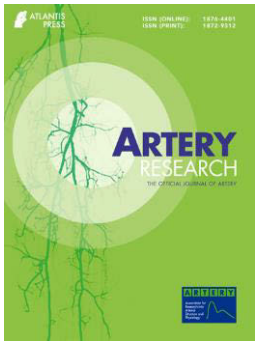

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P2.26: DYNAMIC ASSESSMENT OF VASCULAR RESISTANCES IN DIABETIC MICEUSING A NON-INVASIVE NMR IMAGING APPROACH

J.C. Ménard, E. Giacomini, C. Baligand, D. Bertoldi, P.G. Carlier

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from the brachial artery would be an acceptable substitute for the AO in the VaMoS computations.
Pulsatile diameter change in the AO was registered with aid of a wall track system, and pressure curves measured simultaneously in the AO and the brachial artery with aid of Millar catheters in healthy volunteers (n= 29, 23-72 years).
There were significant differences in 4 out of 6 aortic wall parameters when pressure curves from brachial artery was compared with AO, emphasizing that the VaMoS computation is sensitive to the pulse wave form and that pressure curves in the brachial artery is not an acceptable substitute for the AO when using VaMoS. A transfer function between the brachial and AO pressure curve form might lead to more accurate results.
[1] Stålhand J. 2008; DOI 10.1007/s10237-008-0124-3

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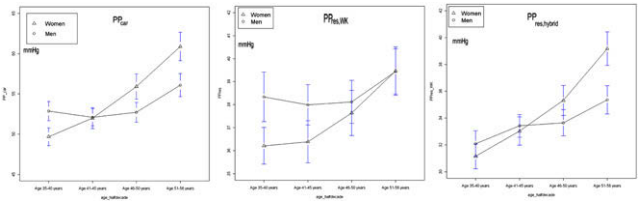
P2.23
THE RESERVOIR PRESSURE CONCEPT: THE 3-ELEMENT WINDKESSEL MODEL REVISITED? APPLICATION TO THE ASKLEPIOS POPULATION STUDY

S.J. Vermeersch [1], E. Rietzschel [2], M.L. De Buyzere [2], D. De Backer [3], G. De Bacquer [3], L.M. Van Bortel [4], T.C. Gillebert [2], P.R. Verdonck [1], P. Segers [1].
[1] *IBItech, Ghent University, Gent, Belgium*
[2] *Department of Cardiovascular Diseaseses, Ghent University Hospital, Gent, Belgium*
[3] *Department of Public Health, Ghent University Hospital, Gent, Belgium*
[4] *Heymans Institute of Pharmacology, Ghent University Hospital, Gent, Belgium*

Background: Traditionally the arterial system is either modelled as a lumped-parameter windkessel model, or as a wave system. Recently, a hybrid model has been proposed in which the arterial system is considered to be a reservoir while still allowing for superimposed wave phenomena. We applied this novel approach to non-invasively obtained carotid pressure waveforms from 2024 subjects from the Asklepios population to investigate the contribution of reservoir pressure to pulse pressure with age and gender and compared it to the windkessel pressure obtained from a more traditional 3 element windkessel model approach.
Methods: $PP_{res,WK}$ and $PP_{res,hybrid}$ were determined by applying a 3-element windkessel model and the hybrid reservoir pressure concept to scaled carotid artery tonometry readings, respectively. The evolution of PP_{car}, $PP_{res,WK}$ and $PP_{res,hybrid}$ was separately examined for men and women after stratification of the population into age quartiles.
Results:



Discussion: PP_{car} increased with age regardless of sex, but was more pronounced in women. This increase is largely due to reservoir pressure, regardless of the model used. Hybrid model results closely resemble those obtained by a 3 element windkessel model, with a strong correlation (r=**, P<0.001) between $PP_{res,WK}$ and $PP_{res,hybrid}$.

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P2.24
ESTIMATION OF ARTERIAL MECHANICAL PROPERTIES BASED ON A PATIENT SPECIFIC WAVE PROPAGATION MODEL

C.A.D. Leguy [1], P. Boutouyrie [3], E.M.H. Bosboom [1], E. Bozec [3], L. Simons [1], A.P.G. Hoeks [2], F.N. Vosse [1].
[1] *1Eindhoven University of Technology, Eindhoven, Netherlands*
[2] *Cardiovascular Research Institute Maastricht, Maastricht, Netherlands*
[3] *3Department of Pharmacology and INSERM U 652, Paris, France*

Background: Arterial stiffness can be assessed using pulse wave velocity (PWV). However, distance measurement introduces an error and an average PWV is considered although arterial stiffness increases distally. A patient specific one-dimensional wave propagation model may reveal details of pressure wave propagation phenomena and mechanical properties of arteries.
Methods: For 6 healthy volunteers, ultrasound wall distension (WD), blood pressure (BP) waveform and blood velocity were assessed at 5 positions along the leg. Blood volume flow (BVF) for each position was estimated assuming Womersley profile. The Young's moduli and diameters of the arteries were derived from the BP and WD. The BVF at the iliac artery (IA) is used as input for the simulations. The in-vivo results were compared with simulated BVF and BP curves to adapt the model parameters iteratively.
Results: The group average diameter equals 7.4±0.6 for the IA, 1.9±0.8 for the posterior tibial (PTA) and 1.7±0.5mm for the pedal (PDA) artery. The ratio IMT/diameter increases along the arterial tree, from 7.5% to 21.1% and 27.5% in the IA, PDA and PTA, respectively. The distensibility equals 0.39±0.07 and 0.36±0.09MPa^{-1} at the IA and PDA; the PWV over IA to PDA segment is 7.4±1.0m/s. The distensibility resulting from the iterative method is 20% smaller than the first estimate based on the measurements while the PWV was the same.
Conclusion: The results show that the shape of simulated BVF is comparable with in-vivo estimations and that the wave propagation model can be used to estimate more accurately arterial mechanical properties.

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P2.25
MATHEMATICAL MODELLING OF THE SYSTEMIC CIRCULATION: INVESTIGATING PRESSURE AND FLOW THROUGHOUT THE MICROCIRCULATION

G.A. Vaughan [2], M.S. Olufsen [3], N.A. Hill [2], C.A. Sainsbury [1].
[1] *BHF Glasgow Cardiovascular Research Centre, Glasgow, United Kingdom*
[2] *Department of Mathematics, University of Glasgow, Glasgow, United Kingdom*
[3] *Department of Mathematics, North Carolina State University, Glasgow, United Kingdom*

An early pathological process common to many vascular diseases is dysfunction of the small arteries. A variety of mechanisms are implicated including endothelial dysfunction. The final common pathway linking these functional pathologies to clinically significant disease is alteration of haemodynamic characteristics of the microcirculation, including the generation of small arteries at which the majority of the pre-capillary pressure drop occurs (resistance arteries).
We have extended a model of the systemic arterial system into the microcirculation. The model is divided into two parts: one comprising the larger arteries and one comprising the smaller arteries, coupled together through an outflow boundary condition at the terminals of the larger arteries. Blood flow and pressure in the larger arteries are predicted from a nonlinear 1D cross-sectional area-averaged model based on the Navier–Stokes equation. Inflow is ascending aortic flow measured using MRI. Small arteries in vascular beds are modelled as an asymmetric structured tree. Impedance is calculated throughout the asymmetric tree, allowing pressure and flow to be calculated at each vessel generation. Physical properties (dimensions, compliance etc) can be altered independently at each vascular generation of the microvasculature.
Using this model, we are able to simulate resistance artery pathologies identified as potential precursors of systemic disease. A detailed theoretical understanding of the haemodynamic impact of such resistance artery pathology on systemic blood flow and pressure has multiple potential uses. Current hypotheses concerning the pathophysiology of very early vascular disease eg 'essential' hypertension may be tested in silico and new hypotheses could potentially be generated.

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P2.26
DYNAMIC ASSESSMENT OF VASCULAR RESISTANCES IN DIABETIC MICEUSING A NON-INVASIVE NMR IMAGING APPROACH

J.C. Ménard, E. Giacomini, C. Baligand, D. Bertoldi, P.G. Carlier.
AIM - CEA NMR Laboratory, Institute of Myology, Pitie-Salpetriere University Hospital, Paris, France

The dynamic determination of peripheral vascular resistances requires simultaneous determination of organ perfusion and systemic arterial blood pressure (BP). We developed an integrated Nuclear Magnetic Resonance (NMR) approach combining measurements of systolic and diastolic BP with tissue perfusion by NMR-Imaging using Arterial Spin Labeling technique (NMRI-ASL) in small animals. This allowed non-invasive determination of local peripheral resistances *in vivo*. As a first example of application, we assessed the vascular conductance in skeletal muscle of type-2 diabetic mice.

Experiments were performed on a Bruker 4T NMR system using a custom-developed setup adapted to small animal investigations.
Tissue perfusion quantification in *gastrocnemius* of mice was performed with a NMR sequence combining fast imaging with ASL[1]. It uses magnetically-labeled blood water as an endogenous tracer to quantify perfusion.
NMR method to determine BP is based on the sphygmomanometric principle: the caudal artery of the mouse was subjected to an external pressure from a tail air cuff. Arterial inflow signal was collected by single-slice dynamic NMR angiography and analyzed by reference to air pressure in the tail cuff.
These hemodynamics parameters were measured during reactive hyperemia after arterial occlusion in 10-week-old male db/db diabetic mice (n=17) and controls (n=14).
Using our dynamic NMR approach, we found both decreases in mean BP (68±9 vs 91±15 mmHg; $p<0.05$) and maximal perfusion (82±19 vs 105±38 $ml.min^{-1}.100g^{-1}$ $p<0.05$) in young db/db mice. However, we found that their maximal vascular conductance was not altered (1.22±0.3 vs 1.27±0.7 $ml.min^{-1}.100g^{-1}.mmHg^{-1}$), hence the relevance of our integrated approach.
1-Raynaud MRM 2001

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P2.27
MECHANICAL MODELING OF IN VIVO HUMAN CAROTID ARTERIES FROM NON-INVASIVE CLINICAL DATA

I. Masson [1], P. Boutouyrie [2], S. Laurent [2], J.D. Humphrey [3], M. Zidi [1].
[1] *CNRS UMR 7054, University Paris 12, Créteil, France*
[2] *HEGP Department of Pharmacology & INSERM UMRS 872, Paris, France*
[3] *Department of Biomedical Engineering, Texas A&M University, College Station, USA*

Background: For mechanical modeling, in vivo data are relatively incomplete in comparison to in vitro results. However, identification of mechanical properties from human clinical data to compute wall stress fields can play an important role in understanding better pathological evolutions.
Aim: Demonstrate the feasibility of material identification and stress computation from clinical data.
Methods: In vivo human common carotid arteries (CCAs) were explored non-invasively. During several cardiac cycles, medial diameter, intimal-medial thickness and blood pressure were measured by a high-resolution echotracking (Art.Lab®) and applanation tonometry (SphygmoCor®), respectively. To study the wall mechanical behavior, the CCA was assumed to be a thick-walled, three-dimensional cylinder subjected to dynamical intraluminal pressure and perivascular constraints. We also assumed a nonlinear, hyperelastic, fiber-reinforced, incompressible material with smooth muscle activity and residual stresses. We included wall mechanical contributions by micro-constituents: an elastin-dominated matrix, collagen fibers, and vascular smooth muscle. We solved the in vivo boundary value problem semi-analytically to compute the intraluminal pressure during a cardiac cycle. Minimizing the difference between computed and measured inner pressures over the cardiac cycle provided the identification of optimal model parameters employing a nonlinear regression. Illustrative data were from two healthy subjects.
Results: The fit-to-data gave very good results. The predicted radial, circumferential, and axial stretches and stresses within the wall during the cardiac cycle were sensible.
Conclusion: We were able to identify experimentally unknown geometric and material parameters directly from in vivo human data. We can extend the proposed approach to pathological cases such as hypertension.

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P2.28
DEVELOPMENT AND VALIDATION IN FLOW-PHANTOMS OF A SIMPLE ULTRASOUND-BASED METHOD FOR ESTIMATION OF WALL SHEAR STRESS IN-VIVO

P.R. Hoskins, J. Blake, W.J. Easson.
University of Edinburgh, Edinburgh, United Kingdom

Background: Wall shear stress (WSS) is an important measure of endothelial function however there are few clinical studies due to lack of a widely available measurement technique.
Aim: To develop and validate a simplified technique for estimation of WSS.
Methods: The Womersley equations were used; these describe pulsatile blood flow. With input of the vessel diameter (from B-mode ultrasound) and the centre-line blood velocity waveform (from Doppler ultrasound), the equations provided velocity profile as a function of time. Wall shear rate was estimated from the velocity gradient at the vessel wall. WSS was estimated from WSR*(viscosity), with an assumed viscosity of 4mPas. The technique was validated in a pulsatile flow phantom for vessels of physiological depth, diameter and flow-waveform.
Results: Estimated mean WSS was in error by 9±1% for brachial, 7±1% for carotid, 22±4% for femoral and 17±10% for fetal aorta.
Discussion: The errors are comparable with those obtained using dedicated WSS measuring systems. The method assumes that the vessel is rigid, straight and that flow is fully developed. There are several arteries where these flow conditions might hold, in health and in early disease where lumen diameter is preserved through outward remodelling. In-vivo validation is needed, possibly against a 'gold-standard' of MRI and computational fluid dynamics.
Conclusion: A simple method for estimation of WSS has been developed which is suitable for clinical studies.
Acknowledgement: The work has been published (Ultrasound Med Biol 2008, 34, 760-774) and previously presented (British Medical Ultrasound Society meeting, UK, December 2007)

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P2.29
AN IN SILICO MODEL OF THE ROLE OF ELASTIN ON GEOMETRY AND BIOMECHANICAL PROPERTIES OF ARTERY IN WILLIAMS BEUREN SYNDROME

L. Hua, V. Louvet, E. Grenier, F. Gueyffier, B. Kassai.
EPICIM/HCL, Centre d'Investigation Clinique 201/INSERM, UCB Lyon I/ UMR5558, Lyon, France

Arteriopathy in Williams-Beuren syndrome (WBS) patients with elastin gene deletion represents the most important mortality and mobidity causes and seems directly correlated with elastin quantity. There is a need for a comprehensive model that accounts for the quantity of elastin and its role in the geometry and biomechanical properties of artery. Such model might improve our understanding of the pathophysiology and improve innovation in drug development for WBS. We present an *in silico* model for the adaptation of human carotid artery in response to elastin deficiency. The model is based on the hypothesis that elastin deficiency-induced growth and remodelling occurs via the excessive production of vascular smooth muscle cells (VSMCs), change in collagen engagement, and increased laminar units to ensure that the average stress of lamina unit in the homeostatic state is unchanged under normal condition. Using an elastin-stress driven model and a constituents-based model, which considers the contributions of elastin, collagen, and VSMCs in an explicit form, we illustrate capabilities of the model in predicting the arterial thickness and biomechanical properties with varying elastin quantity before and after elastin restoration. Alternatively, the model has the potential to estimate, indirectly, the fraction of remaining elastin using the values of arterial thickness and mechanical properties. Our model provides a new approach for mathematically assessing the arterial growth and remodelling in human vascular disease with insight into the importance of constituent distributions.

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P2.30
SERUM FATTY ACID COMPOSITION AS MEDIATORS OF AORTIC PULSE WAVE VELOCITY'S IMPACT ON MORTALITY

S.G. Anderson [1], T.A.B. Sanders [2], J.K. Cruickshank [1].
[1] *The University of Manchester, Manchester, United Kingdom*
[2] *King's College London, London, United Kingdom*

Aims/Hypothesis: Aortic stiffness predicts all-cause and cardiovascular mortality in essential hypertension, diabetes and the community. Potential intermediaries in this relationship include serum fatty acids (FA). We examined whether serum FA influenced aortic stiffness, measured as pulse wave velocity (aPWV), and its impact on mortality.
Methods: After randomly sampling population registers, 174 nondiabetic participants had fasting blood samples and a 75g glucose challenge (GTT), measures of doppler-derived aortic PWV and then serum FA composition determined by HPLC. Mortality data over 18 years' follow-up were obtained via the national registry and principal component (PC) analysis used for statistical modelling.
Results: Docosahexaenoic acid (DHA; $\rho = -0.22$; $p = 0.02$) and Arachidonic acid (AA; $\rho = -0.25$; $p<0.001$) were inversely related to PWV. PC analyses, including 10 measured serum FAs, ethnicity, age and sex, identified five