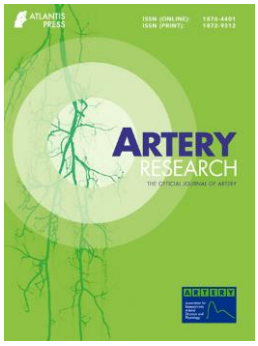

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P5.11: ROLE OF PRESSURE-DEPENDENT ARTERIAL OMPLIANCE IN MODULATING THE PHASE OF WAVE REFLECTIONS: IMPLICATIONS FOR LV-AS COUPLING

Timothy Phan*, John Li

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P5.7
A DATABASE OF VIRTUAL HEALTHY SUBJECTS AS A NEW TOOL TO ASSESS PHYSIOLOGICAL INDEXES AND ALGORITHMS BASED ON WAVE PROPAGATION

Marie Willemet *, Phil Chowienczyk, Samuel Vennin, Jordi Alastruey
King's College London, London, UK

Many physiological indexes and algorithms based on pulse wave analysis have been suggested in order to better understand the physiology of arterial hemodynamics (e.g. pulse wave velocity, transfer functions for central blood pressure derivation). Because these tools are most often computed from hemodynamic measurements, their validation is time-consuming and biased by measurement errors.
We present a new methodology to assess theoretically these computed tools. We create a database of virtual healthy subjects using a numerical 1D-0D model of the arterial hemodynamics, which parameters are varied to cover a physiological healthy range. The generated set of simulations encloses a wide selection of possible cases that could be encountered in a clinical study.
We illustrate this new concept by assessing the efficiency of indexes estimating aortic stiffness, such as central and peripheral foot-to-foot pulse wave velocities computed with different methods (foot-to-foot, sum of squares), the stiffness index and the augmentation index. We also apply our methodology to a new algorithm that estimates the central aortic pressure from peripheral measurements. We show that the results of our analysis confirm clinical observations.
Our database of virtual subjects could become a new tool for the clinician: it provides insight into the physical mechanisms that are important when designing large cohort clinical studies, analyzing their results, and explaining the correlations observed in clinical practice.

P5.8
TOWARDS IN VIVO BIAXIAL CHARACTERISATION OF CAROTID ARTERY MECHANICS

Robert Holtackers *, Bart Spronck, Maarten Heusinkveld, Geneviève Crombag, Jos Op 't Roodt, Tammo Delhaas, Eline Kooi, Evelien Hermeling, Koen Reesink
CARIM School for Cardiovascular Diseases, Maastricht University, Maastricht, The Netherlands

Background: The relative content and loading of collagen and elastin in the arterial wall determine *in vivo* longitudinal pre-stretch. Assessment of arterial distensibility at varying longitudinal pre-stretch could improve characterisation of arterial collagen-elastin matrix properties. We introduce a technique to impose extra longitudinal pre-stretch (Δstretch) to the carotid artery *in vivo* and investigate whether we can predict Δstretch from ultrasound distensibility measurements using a constitutive model.
Methods: In 11 healthy volunteers (22±3 yrs, mean±SD, 6m/5f) we obtained right common carotid artery bifurcation-to-bifurcation length by phase-contrast MR-angiography in two positions: head facing forward (relaxed, R) and head facing up and rotated to the left (stretched, S). We estimated Δstretch from the MR images by two independent operators (Bland-Altman inter-operator bias = 0.5±3%, mean±2SD). Additionally, we obtained brachial blood pressures and carotid diameter-distension (considered as cross-sectional area) by ultrasound echo-tracking. We fitted a constitutive model [Spronck *et al.*, AJP-Heart 2015] to average single-exponential pressure-area curves for both R and S states. We predicted Δstretch using the model, assuming constant axial force over the cardiac cycle.
Results: MRI-estimated Δstretch was +2% while constitutive model-predicted Δstretch was +6%. To check these estimates, we additionally predicted Δstretch based on echo-derived intima-media-thickness measurements, yielding +6%.
Conclusion: Measured and predicted Δstretch values were of the same order of magnitude. Assessment of carotid artery distensibility at varying longitudinal pre-stretch could improve model-based *in vivo* assessment of arterial wall collagen-elastin matrix properties, which are relevant in age- and disease-related arterial remodelling.

P5.9
CARDIAC AND ARTERIAL CONTRIBUTION TO BLOOD PRESSURE CHANGES WITH AGE

Elira Maksuti [1,*], Nico Westerhof [2], Berend Westerhof [3,4], Michael Broomé [1,5], Nikos Stergiopulos [6]

[1]*KTH Royal Institute of Technology, Stockholm, Sweden*
[2]*VU University Medical Center, Amsterdam, The Netherlands*
[3]*Edwards Lifesciences BMEYE, Amsterdam, The Netherlands*
[4]*Academic Medical Center, Amsterdam, The Netherlands*
[5]*Karolinska University Hospital, Solna, Sweden*
[6]*Ecole Polytechnique Fédérale de Lausanne, Lausanne, Switzerland*

During aging, systolic blood pressure (Ps) continuously increases over time, whereas diastolic pressure (Pd) first increases and then slightly decreases after middle-age. These pressure changes are usually explained by changes of the arterial system alone (increase in arterial stiffness and vascular resistance). However, we hypothesize that the heart contributes to the age-related blood pressure progression as well. In this study we quantified the blood pressure changes in normal aging by using the Windkessel model for the arterial system and the time-varying elastance model for the heart, and validated the results against data from the Framingham Heart Study. Arterial changes during aging were prescribed based on literature values, whereas the cardiac changes were computed through physiological rules (compensated hypertrophy and preservation of end-diastolic volume). Results showed that, when accounting for arterial changes only, the Ps and Pd did not conform to the population data. The computed Ps changed from 100 to 122 mmHg and Pd from 76 to 55 mmHg, respectively. When taking cardiac adaptations also into account, Ps and Pd changed from 100 to 151 mmHg and 76 to 69 mmHg, respectively. Our results show that not only the arterial system, but also the heart significantly contributes to the development of blood pressure during aging. The changes in arterial properties initiate a systolic blood pressure increase, which in turn initiate a cardiac remodeling process, further contributing to the development of Ps and Pd.

P5.10
CHANGES IN MECHANICAL PROPERTIES OF FEMORAL ARTERY WALLS IN PIG MODEL OF ARTERIOSCLEROSIS

Robert Pasławski
Medical University Wrocław, Wrocław, Poland

Arteriosclertic lesions leading to increased stiffnes of the walls. The goal of the research was to estimate changes in the mechanical properties of femoral artery in swine with experimentally induced arteriosclerotic changes by western type diet.
Methods: 32 white female pigs (40 kg), were divided into 3 groups: 1) 12 control pigs 2) 10 "diet" pigs fed a "western diet" 3) 10 pigs "regression" — fed a western diet for 9 months and then a standard diet for 3 months. Femoral arteries samples were stained HE method for histopathology, were tested for collagen and elastin content and mechanical properties. Arteriosclerotic changes were classified using 8 class scale (Stary et all. 2000). Mechanical test were conducted using Synergie 100 machine with force sensor MTS (mesurement range 0÷500 N). Thickness of artery wessels was measured by mikroskope SteREO Discovery V20 (Zeiss). Data were analysed statistically using the Statistica 10.0 software.
Results: 2 pigs in Diet group and 4 pigs in Regression group have arteriosclerotic plaque I and II grades. Mechanical indexes: σL Lagrangian stresses, ε Green strain, σ Cauchy stress, ES secant module and Et tangent modulus were not changed.
Conclusion: Despite presence of arteriosclerotic leasions iduced by feeding swine of western type diet, we not seen significant differences in mechanical properties of femoral artery in comparison to standard fed pigs.

P5.11
ROLE OF PRESSURE-DEPENDENT ARTERIAL OMPLIANCE IN MODULATING THE PHASE OF WAVE REFLECTIONS: IMPLICATIONS FOR LV-AS COUPLING

Timothy Phan *, John Li
Rutgers University, Piscataway, NJ, USA

Background: Arterial compliance is pressure-dependent due to the nonhomogeneous composition of the arterial wall. Wall distending pressure varies within each cardiac cycle, thus arterial compliance is dynamic and time-varying within any given cycle. As compliance is a component of the pulsatile load presented by the arterial system (AS), its dynamic nature is expected to influence the phase of wave reflections. This phase modulation of wave reflection may influence left ventricular (LV) and AS coupling.
Methods: A time-varying elastance-resistance model the LV is coupled to a tube-load model of the AS. The tube, representing a segment of the aorta, is uniform and loss-free, terminating in a complex frequency-dependent load incorporating pressure-dependent compliance (C(P)). Aortic

characteristic impedance, pulse wave velocity, and steady afterload were kept constant. In one set of experiments, the magnitude of C(P) was decreased while retaining its pressure-dependence, thus preserving compliance variations within any given cycle. In a second set, both the magnitude and pressure-dependence were progressively decreased, such that compliance became increasingly constant; mean compliance and reflection magnitude were pairwise matched to each case of the first set of experiments.
Results: When stiffening was accompanied by retained pressure-dependence, there was marked delaying of wave reflections compared to more constant compliance cases. Pressures and myocardial wall stress at end-systole were elevated, while stroke volume and ejection period were decreased.
Conclusion: The dynamic loading effects of pressure-dependent compliance can have complex effects on LV-AS coupling. Characterization of the complex changes of C(P) with age and disease deserves further investigation.

P5.13
ESTIMATION OF CENTRAL SYSTOLIC PRESSURE: ARE PERIPHERAL WAVEFORMS AND TRANSFER FUNCTION NECESSARY?

Denis Chemla [1,*], Sandrine Millasseau [2], Edmund Lau [3], P. Attal [4], Alain Nittenberg [1]
[1]*APHP, Kremlin-Bicetre, France*
[2]*Pulse Wave Consulting, St Leu La Foret, France*
[3]*Sydney Medical School, Camperdown, NSW, Australia*
[4]*Shaare-Zedek Medical Center and Hebrew University Medical School, Jerusalem, Israel*

Background and aim: The degree of systolic pressure amplification (SPamp) from aorta to brachial artery depends on a number of variables including age, gender, heart rate and arterial stiffness. It is admitted that central systolic blood pressure (cSBP) cannot be predicted with sufficient accuracy from brachial blood pressure and thus needs to be estimated using peripheral waveform analysis and transfer functions. We have developed a proprietary method for direct central blood pressure (DCBP) estimation, which challenges this paradigm. In the present preliminary study, our DCBP method was applied to a meta-analysis of published studies with invasive, high-fidelity pressure tip data of both aortic and brachial artery pressures.
Methods and results: Five studies were found fulfilling our criteria. There were 282 subjects (77.3% male), with known or suspected coronary artery diseases. Mean age was 63.3±13.2years and heart rate was 67.1±11.3bpm. Invasive brachial systolic, diastolic and mean BP were 137.9±19.9mmHg, 70.9±10.2mmHg and 97.1±11.7mmHg, respectively. The measured invasive cSBP was 131.1±19.9mmHg and the mean SPamp was 6.8mmHg. The cSBP estimated with DCBP method was 132.9mmHg and the mean difference with invasive measures was 1.8mmHg.
Conclusion: The meta-analysis of studies documenting invasive high-fidelity pressure at aortic and brachial artery level indicates that our DCBP method can predict cSBP from brachial blood pressures with good accuracy in relatively old subjects with established or suspected coronary diseases. Further studies are needed to document the precision of the DCBP method in healthier and younger subjects as well as its sensibility to peripheral BP measuring method.

P5.14
THIGH-CUFF BASED MEASUREMENT OF AORTIC PULSE WAVE VELOCITY: INITIAL TESTING OF A NOVEL VASERA PROTOTYPE DEVICE

Francisco Londoño [1,*], Daime Campos [1], Shigeo Horinaka [1], Julio Chirinos [2], Patrick Segers [1]
[1]*Ghent University, Gent, Belgium*
[2]*University of Philadelphia, PA, USA*

Introduction: Fully automated cuff-based devices have been developed for the assessment of arterial stiffness via pulse wave velocity (PWV) measurement, such as the VaSera device (Fukuda Denshi). To date, measurements were confined to the heart-to-ankle segment, yielding PWV and stiffness indices that are not easily inked to carotid-femoral PWV (cf-PWV), the presumed reference for measurement of aortic PWV.
Methods: We performed initial tests (N=14, 9 males, mean age 27.4±3.3, BMI 23.8±3.4) using a novel thigh-cuff prototype that can be used as a substitute for the ankle cuffs in the VaSera device. Extracted data included heart-thigh (ht-PWV) and heart-ankle (ha-PWV). cf-PWV was obtained using ultrasound (GE Vivid 7) on the right side.
Results: Measurements were successfully obtained for all subjects. cf-PWV was 5.32 ± 0.43 m/s. ha-PWV was 6.35±0.49 m/s, and was significantly higher than cf-PWV (paired t-test; $P<0.001$). ht-PWV, on the other hand, was 5.51±0.50 m/s and was not significantly different from cf-PWV. Bland-Altman analysis demonstrated a non-significant bias of 0.19±0.54 m/s of ht-PWV with respect to cf-PWV.
Conclusion: We conclude that, in this small-sized young and healthy population, fully automated measurement of heart-thigh PWV is straightforward and easy. Measured values were not different from carotid-femoral PWV. Further research is warranted to confirm these findings in a larger population spanning a large age range and cardiovascular risk profiles.

P5.15
EVALUATION OF AORTIC ^{18}F-NAF TRACER UPTAKE DETECTED USING PET/CT IN PREDICTING AORTIC CALCIFICATION OVER A 4-YEAR FOLLOW-UP PERIOD

Marina Cecelja [*], Amelia Moore, Ignac Fogelman, Michelle Frost, Phillip Chowienczyk
King's College London, London, UK

Background: Uptake of ^{18}F-sodium fluoride (^{18}F-NaF) in the aortic wall may reflect metabolically active areas of calcification, an important predictor of cardiovascular morbidity and mortality when detected by computed tomography (CT). The aim of this project was to determine if ^{18}F-NaF uptake in the aorta can predict development of calcification as detected by CT.
Method and results: Twenty one postmenopausal women (mean age 62±6 years, range 52-74), underwent assessment of aortic ^{18}F-NaF uptake using positron emission tomography/computer tomography (PET/CT) at baseline and after a mean follow-up of 3.7±1.3 years. Tracer uptake was quantified by calculating the target-to-background ratios (TBR). At baseline, there was a trend to a positive correlation between CT calcium volume score and tracer uptake ($r=0.33$, $P=0.15$). Over the follow-up period aortic CT calcium volume increased from 0.45±0.62 to 0.71±0.93 cm^3 ($P<0.04$). However, the change in calcium volume did not significantly correlate with baseline TBR values ($r=0.18$, $P=0.52$). TBR at baseline did not differ between participants with ($n=16$) compared to those without ($n=5$) progression in calcium volume progression (2.43±0.46 vs. 2.31±0.38, $P=0.58$). In aortic segments identified to have highest tracer uptake at baseline, calcium volume did not significantly change over the follow-up period (from 0.08±0.15 to 0.12±0.26 cm^3, $P=0.42$). In multivariate regression analysis baseline TBR did not associate with progression in calcium volume.
Conclusion: In a cohort of postmenopausal women ^{18}F-NaF uptake as measured by TBR was not a predictor of progression of aortic calcification as detected by CT over a 4-year follow-up period.

P5.17
CAROTID PULSE PRESSURE ASSESSMENT BY MEANS OF AN ACCELEROMETRIC SENSOR

Nicole Di Lascio [1,2,*], Vincenzo Gemignani [2], Rosa Maria Bruno [2], Elisabetta Bianchini [2], Francesco Stea [2,3], Lorenzo Ghiadoni [3], Francesco Faita [2]
[1]*Institute of Life Science, Scuola Superiore Sant'Anna, Pisa, Italy*
[2]*Institute of Clinical Physiology, National Research Council, Pisa, Italy*
[3]*Department of Internal Medicine, University of Pisa, Pisa, Italy*

Central pulse pressure (cPP) is increasingly investigated as possible independent predictor of cardiovascular risk and carotid pulse pressure (carPP) can be used as a surrogate marker of cPP. Despite its importance, carPP measurement remains challenging in clinical practice. The aim of this study was to introduce a new easier-to-use method for non-invasive carPP evaluation based on an accelerometric sensor.
Accelerometric signals were recorded in 22 subjects (males: 45.5%, 47.4±17 years, hypertension: 50%; smoking: 18%; diabetes: 23%; hypercholesterolemia: 27%). Under the hypothesis that these signals represent the acceleration linked to the displacement of the carotid near wall, $carPP_{acc}$ values were achieved double integrating the accelerometric waveforms and calibrating the obtained diameter curves with brachial pressure measurements. $carPP_{acc}$ measurements were compared with tonometric assessments ($carPP_{ton}$). Moreover, accelerometric carotid pressure waveforms (P_{acc}) were contrasted in terms of shape to those obtained by tonometry (P_{ton}), calculating the root mean square error ($RMSE_{ton}$) and the regression coefficients (r_{ton}).
$carPP_{acc}$ values (46±10.55 mmHg) were significantly correlated with $carPP_{ton}$ (47.5±11.2 mmHg) assessments ($R=0.93$, $p<0.001$). The Bland-Altman analysis provided a non-significant bias of -1.54 mmHg. The validity of the accelerometric approach was confirmed by morphological parameters ($RMSE_{ton}=5±1.95$ mmHg; $r_{ton}=0.94±0.04$).