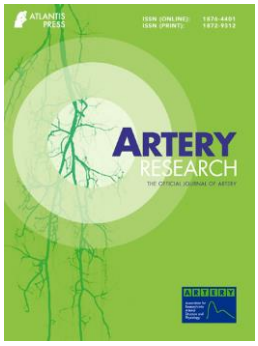

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1.3: IS IT TIME TO QUESTION THE VALIDITY OF IMPEDANCE ANALYSIS?

J. Tyberg, N. Shrive, L. Burrowes, S. Sridharan, C. Bouwmeester, J.-J. Wang

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Oral Presentation Abstracts

1.1
CAROTID ENDOTHELIAL SHEAR STRESS ASSESSED BY 3T-MRI IS ASSOCIATED WITH AORTIC PULSE WAVE VELOCITY IN HEALTHY VOLUNTEERS

R. Duivenvoorden [1], B. van den Boogaard [1], A. G. Holleboom [1], A. J. Nederveen [2], J. S. Lameris [2], J. J. P. Kastelein [1], J. A. Kuivenhoven [1], E. S. G. Stroes [1], E. de Groot [1,3,*]
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Background: Low endothelial shear stress (ESS) elicits endothelial dysfunction. However, the relationship between ESS and aortic pulse wave velocity (PWV), a validated surrogate marker for cardiovascular disease, is unknown in humans. We developed a 3.0 Tesla magnetic resonance imaging (MRI) protocol to assess associations of ESS and PWV in healthy subjects.
Methods: Common carotid 3 T-MRI measurements were performed in 55 subjects (aged 41 ± 15years). Axial gradient echo Phase-Contrast images were acquired over 45 phases per heartbeat, using a 5 cm single-element microcoil, with slice thickness 3 mm, non-interpolated pixel size 0.6 x 0.6 mm, velocity encoding 150 cm/s. The mean ESS in the cardiac cycle was calculated: ESS = μ•WSR, μ is the blood viscosity (3.2 Pa•s), WSR was the slope of the velocities close to the artery wall assessed by second order curve fitting of the velocity profile.
Results: Mean ESS was 0.89(0.23)N/m^2, and PWV was 7.21(1.58)m/s. ESS was inversely correlated with PWV (Pearsons' $r = -0.40$, $p = 0.01$). Multiple linear regression analysis accounting for age, gender and systolic blood pressure revealed that ESS was an independent predictors of the response variable PWV (regression coefficients [b] = −1.67 N/m^2 per m/s, $p = 0.04$).
Conclusion: Our carotid MRI data show that ESS is an important determinant of arterial stiffness in humans. The data warrant further studies to evaluate use of carotid ESS as a non-invasive tool to understand individual CVD risk and to assess novel drug therapies in cardiovascular disease prevention.

1.2
AUGMENTATION INDEX IS NOT A VALID MEASURE OF WAVE REFLECTION WHEN IT IS NEGATIVE AND THIS DISTORTS THE PRESUMED RELATIONSHIP BETWEEN AGING AND WAVE REFLECTION

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Background: The relationship between aging and wave reflection has been disputed [1, 2]. Augmentation index (AI_x) increases with increasing age, however the validity of AI_x as a measure of wave reflection, particularly when AI_x is negative is unknown.
Methods: Measurements of carotid pressure and flow velocity were made in the carotid artery of 65 healthy normotensive individuals (age 21–78 yr; 43 male). AI_x, wave reflection index (WRI) and P_b/P_f were calculated.
Results: AI_x was positively correlated with age (beta (95% CI) = 0.46 (0.19, 0.73); $p = 0.001$). In contrast log WRI and P_b/P_f showed negative associations with age (beta (95% CI) = −0.009 (−0.016, −0.002) $p = 0.01$ and −0.001 (−0.001, −0.000); $p = 0.001$ respectively). AI_x did not correlate with WRI or P_b/P_f, although AI_x and WRI correlated weakly when AI_x was restricted to positive values (rho = 0.35; $p = 0.03$). In contrast log WRI and P_b/P_f were closely correlated ($r = 0.66$; $p < 0.001$). Wave intensity analysis showed that negative augmentation was due to a forward decompression wave in mid systole and was consequently an unreliable indicator of reflected compression waves.
Conclusions: Augmentation index is not a valid measure of wave reflection when it is negative; this is common in younger individuals and distorts the relationship between aging and wave reflection. In healthy normotensive individuals wave reflection in the common carotid artery decreases with increasing age

[1] Namasivayam *et al*. Hypertension. 2009; 53: 979–985.
[2] Vasan. Hypertension. 2008; 51: 33–36

1.3
IS IT TIME TO QUESTION THE VALIDITY OF IMPEDANCE ANALYSIS?

J. Tyberg [1,*], N. Shrive [1], L. Burrowes [1], S. Sridharan [1], C. Bouwmeester [1], J.-J. Wang [2]
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Although the 3-element Windkessel (Wk) is still a useful analogue of arterial hemodynamics, can the validity of the frequency-domain analysis continue to be assumed? Our alternative time-domain approach holds that measured pressure is the sum of a Wk (P_{Wk}) and an "excess" pressure (P_{excess}).
"Characteristic impedance" (Z_0) is critical. Originally called characteristic resistance by Westerhof, Z_0 was simulated like peripheral resistance in a hydraulic model but recently has been interpreted only in the frequency domain. We have shown that P_{excess} varies linearly with aortic inflow with a slope of Z_0. Bench-top experiments with canine peak flows and aortic dimensions yielded pressure drops equal to those measured physiologically, and a proximal resistance approximating Z_0. A bench-top experiment simulating Westerhof's hydraulic circuit demonstrated a P_{Wk} waveform.
We calculated the frequency-dependent impedance of measured pressure, P_{Wk} and P_{excess}, under the influence of nitroprusside (NP) and methoxamine (Mtx). With NP, there was no impedance minimum and the modulus of P_{excess} was frequency-independent. With Mtx, an impedance minimum was demonstrated but was due entirely to P_{Wk}. Thus, the impedance minimum appears to be due only to the P_{Wk} and may not also be essentially related to wave reflection.
Finally, we used our approach to demonstrate positive and negative wave reflection in the canine aorta. However, if P_{Wk} was not initially subtracted, ***backward waves appeared first in the ascending aorta and they appeared to be propagated forward*** (figure).

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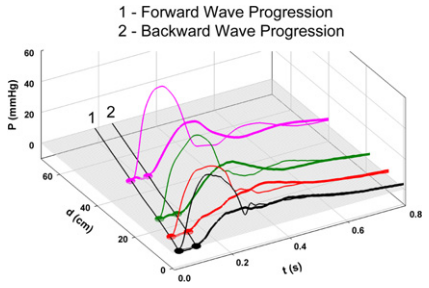

These profoundly paradoxical results above seem to undermine the fundamental presuppositions of the frequency-domain analysis.

1.4
CAN AIX PREDICT ALL-CAUSE MORTALITY IN A GENERAL POPULATION?

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Background: Aortic augmentation Index (AIx) is a measurement of pulse wave reflections and an indirect measure of arterial stiffness. AIx predicts all-cause mortality and CV-mortality in selected patient group with end-stage renal failure and in patients undergoing percutaneous coronary intervention (PCI). The objective of this study was to analyse AIx as an independent predictor of all-cause mortality in a population without known cardiovascular disease (CVD).
Methods: This study is based on 3,432 subjects from the 4th survey of the Copenhagen City Heart Study with AIx measured non-invasively. During follow-up (mean 6.5 years) 334 persons died. AIx was divided in tertiles with the lowest tertile as reference. Mortality risk was analyzed by Cox proportional hazard models with age as the underlying time scale adjusting for heart rate, height, weight, blood pressure, total-cholesterol, smoking, alcohol, diabetes, education, physical activity and predisposition to CVD.
Results: AIx significantly predicted all-cause mortality but in opposite direction for men and women.

	Men		Women	
	HR	95 % CI	HR	95 % CI
AIx — intermediate vs. low tertile	1.86	1.06—3.27	0.66	0.44—0.99
AIx — high vs. low tertile	2.30	1.24—4.24	0.53	0.34—0.82

Conclusion: High AIx was associated with increased mortality in men but decreased in women. The surprising finding in women may be related to gender related difference in the arterial properties measured by AIx as also reflected by AIx reaching a plateau in women approximately ten years earlier than men.
Conclusion: High AIx increased the risk of mortality in men but the opposite was seen in women. This can be explained by a curvilinear AIx/age relationship more pronounced in women where old women may have decreased pulse wave reflections in accordance with findings in the Framingham studies.

1.5
NOVEL NON-INVASIVE METHOD TO ASSESS WAVE REFLECTION FROM THE PRESSURE WAVEFORM ALONE

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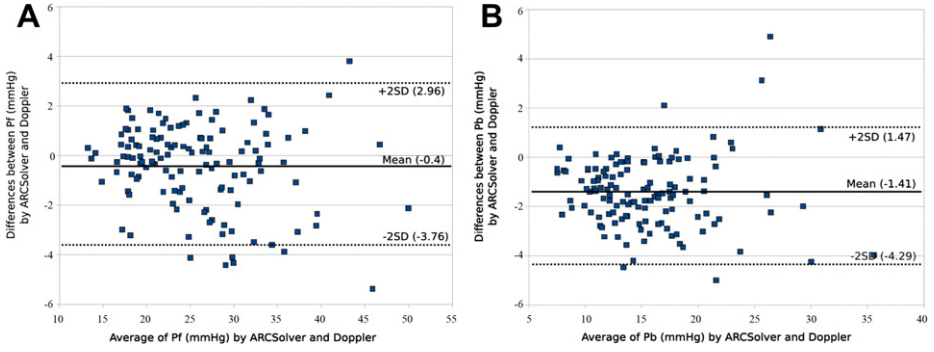
Background/Objectives: Within the last decade the quantification of pulse wave reflections focused on aortic systolic pressure and its augmentation based on analysis of pressure waves alone. A different approach is wave separation analysis (WSA), which quantifies the total amount of arterial wave reflection considering both aortic pulse and flow waves. The aim of this work is the development of an accurate ventricular blood flow model based on central blood pressure waveform for proper WSA and its validation against Doppler ultrasound.
Methods: The introduced ARCSolver method, which grounds on higher order mathematical flow models, describes and implements the outflow of the left ventricle during systole based on a non invasive estimated central pressure waveform. To evaluate the performance of the proposed approach, comparisons against reference Doppler measurements and triangular flow models are made for 131 patients.
Results: Against Doppler the mean difference and standard deviation of the amplitudes of the decomposed forward and backward pressure waves are −0.4 (1.68) mmHg (Fig A) and −1.41 (1.44) mmHg (Fig B). The corresponding mean RMSE for the separated pressure curves is 0.93 (0.51). The results indicate that the ARCSolver method provides accurate estimates of investigated parameters.
Conclusion: The comparison with Doppler ultrasound flow waves as well as recently proposed simple triangular flow waves showed that our approach reduces variability and provides accurate results.



1.6
ON-LINE VISUAL FEEDBACK OF PARALLEL DIAMETER WAVEFORMS IMPROVES QUALITY OF LOCAL CAROTID ARTERY PULSE WAVE VELOCITY MEASUREMENT

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Background: We previously demonstrated that local carotid artery pulse wave velocity (locPWV) can be obtained by high frame-rate multiple M-line ultrasonography. In this study we tested whether on-line display of diameter waveforms improves measurement acceptance rate and reproducibility.
Methods and Results: In 10 volunteers (age 31 ± 14 yrs) we obtained with and without visual feedback multiple M-line scans of the right common carotid artery. Using the dicrotic notch as fiducial point, locPWV was