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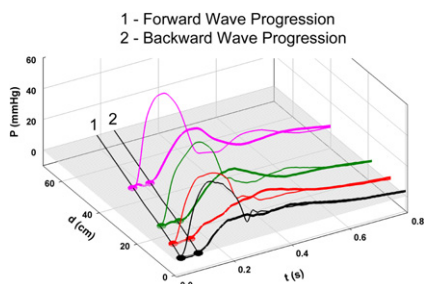
1.6: ON-LINE VISUAL FEEDBACK OF PARALLEL DIAMETER WAVEFORMS IMPROVES QUALITY OF LOCAL CAROTID ARTERY PULSE WAVE VELOCITY MEASUREMENT

K.D. Reesink, F.C.G. van Bussel, J. op 't Roodt, E. Hermeling, A.P.G. Hoeks

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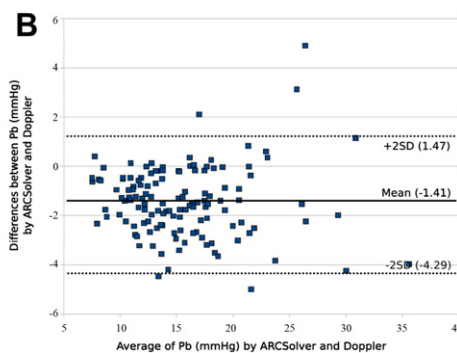
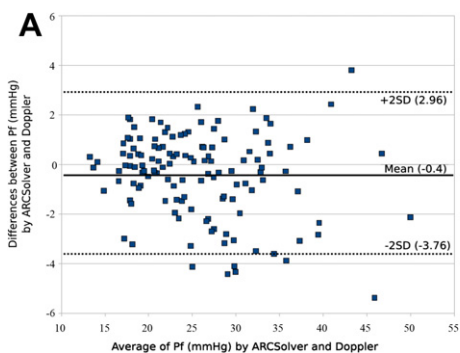
These profoundly paradoxical results above seem to undermine the fundamental presuppositions of the frequency-domain analysis.

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

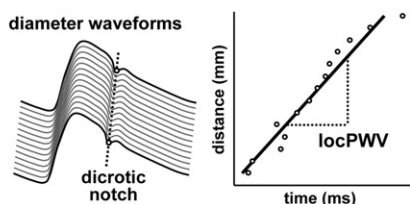
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Background: We previously demonstrated that local carotid artery pulse wave velocity (locPWV) can be obtained by high frame-rate multiple M-line ultrasonography. In this study we tested whether on-line display of diameter waveforms improves measurement 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

calculated as the slope of the regression line between M-line positions and time-points of 14 parallel diameter waveforms (Figure). Beat estimates were accepted when regression root mean square error (RMSE) was below 0.07, 0.10 or 0.15 ms, affecting acceptance rate and within-subject reproducibility (Table). Overall, on-line feedback significantly improved reproducibility by about 50%, enabling good discrimination between subjects: within-subject reproducibility < between-subject SD (Table). LocPWV appeared higher when measured without feedback due to low numbers of estimates in some subjects.

Conclusions: On-line visual feedback improves the quality of local pulse wave velocity measurements. With feedback, an RMSE threshold of 0.10 ms appears optimal in trading off measurement acceptance rate and reproducibility.



feed-back	maxRMSE allowed (ms)	accept. rate (%)	reprod. (m/s)	locPWV (m/s)
yes	0.07	47 ± 29 [#]	0.59 [*]	4.4 ± 2.1 [§]
	0.10	71 ± 33 [#]	0.69 [*]	4.3 ± 2.0 [§]
	0.15	87 ± 31	0.85 [*]	4.3 ± 2.0 [§]
no	0.07	37 ± 24	1.38	5.7 ± 2.5
	0.10	52 ± 26	1.28	5.1 ± 2.5
	0.15	83 ± 31	1.40	5.1 ± 2.0

Values given as mean±SD. *p<0.001, §p<0.03, #p=0.08 yes vs. no.

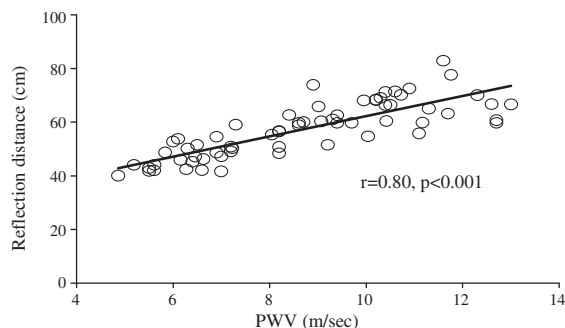
3.1 NEW INSIGHTS INTO ARTERIAL STRUCTURAL-FUNCTIONAL INTERACTIONS AND THE IMPLICATIONS FOR PRESSURE AUGMENTATION IN HUMANS: A META REGRESSION ANALYSIS IN 8336 SUBJECTS

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Introduction: Pressure augmentation is thought to arise as aortic stiffening leads to the progressively earlier return of waves from fixed distal reflection sites. However, several studies dispute this central tenet of pressure augmentation, and instead report variation in reflection site with ageing and arterial stiffness.

Methods: We undertook a meta-analysis to assess the interaction between the aortic reflection site with ageing and arterial stiffness. Systematic literature review was performed to identify studies that published data on Pulse Wave Velocity (PWV) and reflection time, from which we calculated the distance to the reflection site.

Results: We identified 31 studies with 68 cohorts resulting in the inclusion of 8336 subjects (Age 47 ± 13 years). PWV ranged from 4.86 to 13 m/sec, reflection time from 94 to 176 ms and distance 0.40 to 0.82 metres. Reflection time decreased with PWV ($r = -0.74$, $p < 0.001$) and age ($r = -0.72$, $p < 0.001$), whereas reflection distance increased with PWV ($r = 0.80$, $p < 0.001$) and



age ($r = 0.42$, $p < 0.01$). As PWV increased from 4.86–13 m/sec, reflection time decreased by 55ms, far less than predicted (106 ms), whilst the reflection site appeared to move distally by 31 cm. Furthermore, reflection distance did not increase with subject height ($r = 0.12$, $p = 0.37$).

Conclusion: The aortic reflection site is not fixed to an anatomical location, as is widely believed, but instead appears to vary with changes in aortic stiffness and age. This challenges the conventional theory and suggests that wave reflection may not be the principal cause of systolic pressure augmentation.

3.2 A COMPARISON OF THE VICORDER APPARATUS WITH SPHYGMOCOR DEVICE FOR THE NON-INVASIVE ASSESSMENT OF AORTIC BLOOD PRESSURE: AN INVASIVE VALIDATION STUDY

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Background: Aortic/central blood pressure (cBP) is an important determinant of cardiovascular risk. The SphygmoCor device applies a transfer function to radial BP waveforms calibrated to brachial systolic and diastolic BP (bSBP/bDBP) to estimate cBP parameters. Radial waveforms can be also calibrated to brachial mean BP (bMBP) and bDBP. Vicorder is a new cuff-based, operator-independent device which converts bBP waveforms to aortic waveforms to derive cBP.

Objective: to compare cBP estimated by non-invasive (Vicorder & SphygmoCor) devices to invasive cBP at cardiac catheterization.

Methods: Invasive BP (iBP) was measured in 33 patients (59 ± 11 years, 63% males) undergoing diagnostic angiography, with a fluid-filled catheter at the aortic root. Simultaneous measurements were made using Vicorder and SphygmoCor. Brachial waveforms (Vicorder) were calibrated to oscillometric bSBP/bDBP; radial waveforms (SphygmoCor) were calibrated to oscillometric bSBP/bDBP and to bMBP/bDBP.

Results: Average (±SD) bSBP/bDBP was 145(±18)/81(±11) mmHg. iSBP/iDBP was 136/74(±18/9) mmHg; Vicorder-derived cSBP (137 ± 17 mmHg) was in agreement with iSBP (mean BP 0.3 ± 8.0 mmHg, $p = n.s.$), while Vicorder-derived cDBP (81 ± 11 mmHg) was higher than iDBP (mean BP 7.0 ± 7.4 mmHg, $p < 0.001$). SphygmoCor bSBP/bDBP-calibrated cSBP (131 ± 18 mmHg) under estimated iSBP (mean BP -5.7 ± 9.2 mmHg, $p = 0.002$). SphygmoCor bMBP/bDBP-calibrated cSBP was higher than iSBP (141 ± 17 mmHg, mean BP 4.3 ± 7.2, $p = 0.003$).

Conclusions: Vicorder apparatus is highly accurate in non-invasive assessment of cBP compared with catheter-derived iSBP. SphygmoCor bSBP/bDBP-calibrated cSBP was lower than iSBP, while SphygmoCor bMBP/bDBP-calibrated cSBP was higher. Vicorder apparatus provides clinically useful values of cSBP.

