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## **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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## Oral Presentation Abstracts

1.1

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

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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 3T-MRI measurements were performed in 55 subjects (aged  $41 \pm 15$  years). 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  $0.6 \times 0.6$  mm, velocity encoding 150 cm/s. The mean ESS in the cardiac cycle was calculated:  $ESS = \mu \cdot WSR$ ,  $\mu$  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  $0.89(0.23) \text{ N/m}^2$ , and PWV was  $7.21(1.58) \text{ m/s}$ . 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 predictor of the response variable PWV (regression coefficients  $[b] = -1.67 \text{ N/m}^2 \text{ per m/s}$ ,  $p = 0.04$ ).

**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?

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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 ( $P_{\text{excess}}$ ).

“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  $P_{\text{excess}}$  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  $P_{\text{excess}}$ , under the influence of nitroprusside (NP) and methoxamine (Mtx). With NP, there was no impedance minimum and the modulus of  $P_{\text{excess}}$  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).