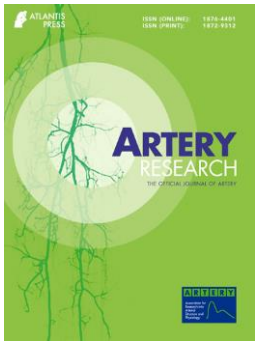

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PO-10: A MULTI-MODALITY 4D SYSTEM FOR ANALYSIS OF THE AORTIC MORPHOLOGY AND FUNCTION FROM MR OR CT

Honghai Zhang, Xiangmin Zhang, Thomas Scholz, Gardar Sigurdsson, Andreas Wahle

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vs. 0.33±0.09, $p>0.05$). Preliminary data in pooled Caucasian (n=3) human umbilical vein endothelial cells (HUVECs) demonstrates greater esRAGE mRNA (qRT-PCR) than AA HUVECs, but similar full-length RAGE mRNA.
Conclusion: These preliminary data suggest that higher sRAGE in Caucasian compared with AA adolescents is likely not from higher esRAGE but a combination of cleavage from non-MMP9 sheddases and alternative splicing of RAGE.

PO-08
EFFECTS OF ACUTE DIETARY NITRATE SUPPLEMENTATION ON AORTIC WAVE REFLECTION IN YOUNG ADULTS

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Objective: Evidence suggests that dietary nitrate supplementation (i.e. beetroot juice) decreases measures of peripheral blood pressure. However, the effects of acute dietary nitrates on central aortic pressures are unclear. Thus, the objective of this study was to investigate the effects of beetroot juice consumption on central aortic pressures and indices of aortic wave reflection.
Methods: 13 healthy, normotensive, non-smoking, untrained young adults (25±1year) consumed 500ml of beetroot juice (BR). High-fidelity radial arterial pressure waveforms using applanation tonometry and venous blood samples were taken at baseline, 60, 90, 120, 150 and 180 minutes post BR consumption (Study 1). Indices of aortic wave reflection (Augmentation Index; AIx and AIx normalized for heart rate; AIx@75bpm) were analyzed using the generated central aortic blood pressure waveforms (SphygmoCor). To control for the potential confound of fluid ingestion on blood pressure, 7 of the subjects came back for an additional study visit which consisted of drinking 500ml of water (Study 2; control trial). Applanation tonometry measurements were performed at the same time points as Study 1.
Results: Study 1: Central systolic pressures were reduced after 90 min following BR (~3-4mmHg; $P<0.05$). Additionally, AIx and AIx@75bpm were reduced at all-time points following BR ($P< 0.05$; Figure 1). Study 2: Compared to the control trial, AIx was lower at all-time points following BR ($P<0.05$). However, AIx@75bpm was only reduced relative to the control condition at 150 and 180 min post consumption ($P<0.05$; Figure 2).
Conclusion: Our data provide evidence that in addition to the beneficial effects on peripheral blood pressures, acute dietary nitrate supplementation (via beetroot juice) also decreases central aortic pressures and wave reflection in young healthy adults. These effects on central aortic hemodynamics appear to be greatest 2.5-3 hours after BR consumption and are likely mediated by an increase in NO bioavailability via nitrate-nitrite-NO pathways.

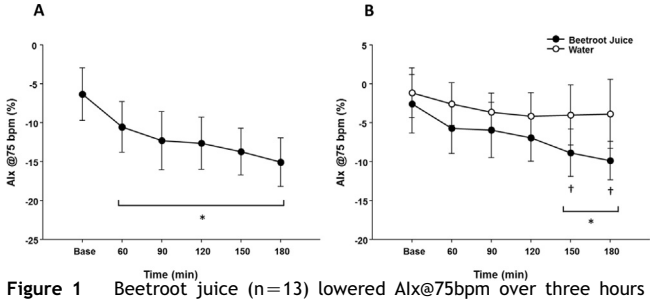

Figure 1 Beetroot juice (n=13) lowered AIx@75bpm over three hours (A; Study 1). When compared to water (control trial; n=7), BR decreased AIx@75bpm at 150 and 180 minutes post consumption (B; Study 2). * $P<0.05$ vs Baseline. † $P<0.05$ vs control.

PO-09
SPIRONOLACTONE AS ADD-ON THERAPY TO CHLORTHALIDONE IMPROVES ENDOTHELIAL FUNCTION, ARTERIAL STIFFNESS AND INSULIN RESISTANCE IN EUROPEAN AND AFRICAN AMERICAN PATIENTS WITH ESSENTIAL HYPERTENSION — A DOUBLE-BLIND PLACEBO-CONTROLLED RANDOMIZED STUDY

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Diuretics have been shown to have a neutral effect on cardiovascular (CV) biomarkers like arterial stiffness and endothelial function despite their blood pressure (BP) lowering effect. Thiazide diuretics generally have harmful effects on glucose metabolism, however, the effect of mineralocorticoid receptor antagonists on insulin resistance in essential hypertension (eHTN) is only partially elucidated. We hypothesized that chlorthalidone (CHT) in combination with spironolactone (SPL) results in better arterial compliance then CHT therapy alone through additional improvement of glucose metabolism parameters.
Methods: This double-blind placebo-controlled randomized single center study aimed to identify SPL add-on therapy to CHT treatment alone on CV risk markers such as BP, 24-h ambulatory blood pressure monitoring (24-H ABPM), aortic BP (aBP), augmentation index (AIx), pulse wave velocity (cfPWV), flow-mediated dilation (FMD), fasting glucose, plasma insulin levels and insulin sensitivity (by homeostasis model assessment: HOMA-IR). A total of 34 patients (21.7% male, 40% white) were randomized to either CHT 25 mg + Placebo or CHT 25 mg + SPL 25 mg once daily. At baseline and after 3 months office BP, 24-H ABPM, markers of arterial stiffness, FMD, fasting glucose, plasma insulin levels and HOMA-IR.
Results: The study showed statistically significant improvements after three months in patients treated with CHT+ SPL in clinic BP, 24-hour ABPM, FMD, markers of arterial stiffness, and glucose metabolism. In detail, clinic SBP (131.5±14.6 to 119.1±14.3 mmHg ($P = 0.034$), aortic SBP (122±13 vs 113±13.7 mm Hg, $p = 0.048$), 24-H ABPM SBP (151.5±15.1 to 131.7 ±10.4 mm Hg, $p=0.0049$, 24-H ABPM DBP 83.2±6.1 to 74 ±9.3 mm Hg, $p=0.032$, 24-H ABPM. Fasting plasma glucose, plasma insulin levels decreased and insulin sensitivity (by homeostasis model assessment: HOMA-IR) improved with SPL as compared to CHT alone ($p<0.001$), AIx (28±9 versus 25.4±6.9 %) and cfPWV (9±2 vs 7.5±1.8 m/s) in the CHT+SPL group. Endothelial function improved significantly in the CHT+SPL group as compared to the control group (5.5 ± 1.7 to 8.8 ± 2.7 ($p = 0.004$)).
Conclusion: These results suggest that SPL as add-on therapy to CHT improves BP, markers of arterial compliance, and glucose metabolism in patients with eHTN, while CHT only therapy may have unfavorable effects. Treatment with SPL additional to CHT may represent a novel approach to improve unfavorable metabolic disturbances and CV risk markers.

PO-10
A MULTI-MODALITY 4D SYSTEM FOR ANALYSIS OF THE AORTIC MORPHOLOGY AND FUNCTION FROM MR OR CT

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Objective: Develop an integrated system for multi-modality 4D (3D+time) aortic data analysis including data construction, interactive pre-segmentation, accurate multi-surface segmentation and refinement, and quantitative index measurement. Provide a graphical user interface (GUI) with intuitive data visualization and workflow control. Test the capabilities of the system on MR and CT data.
Methods: 4D image with isotropic 3D voxels is constructed from DICOM images of a study. Candy-cane and LVOT MR data are fused together to benefit from their combined information. Lumen pre-segmentation is achieved by a few mouse clicks with instant feedback. Lumen (and outer wall for CT) surfaces are segmented in 3D by optimal graph search with embedded geometric constraints that guarantees to be global optimum. The result is refined using approximate clues instead of tediously redrawing individual contours. Quantitative indices — cross-sectional area, eccentricity and distensibility, centerline curvature and motion, wall thickness and calcification volume — are computed from complete 4D aortic surfaces. Due to its modularized design, each component can be independently fine-tuned for performance or extended to handle new modality or imaging protocol. The developed system provides simultaneous visualization of image, volume and surface data. The segmentation and quantitative analysis are guided by GUI with clear instructions and examples.
Results: Preliminary evaluation of segmentation accuracy on 20 dataset (10 MR, 10 CT) showed good absolute surface positioning errors (MR: 1.5±1.4mm, CT: 0.4±0.6mm). The user only needs to specify two aortic end points and several points inside the lumen on one 3D image. The computational time is approximately 20 seconds for 2.5GB 10-phase CT data or 500MB 20-phase MR data.
Conclusion: We develop a multi-modality 4D aorta analysis system with user-friendly interface and powerful segmentation and refinement tools. Various novel quantitative indices are computed from the complete 4D aortic surfaces, thus enabling comprehensive analysis of aortic physiology and morphology.

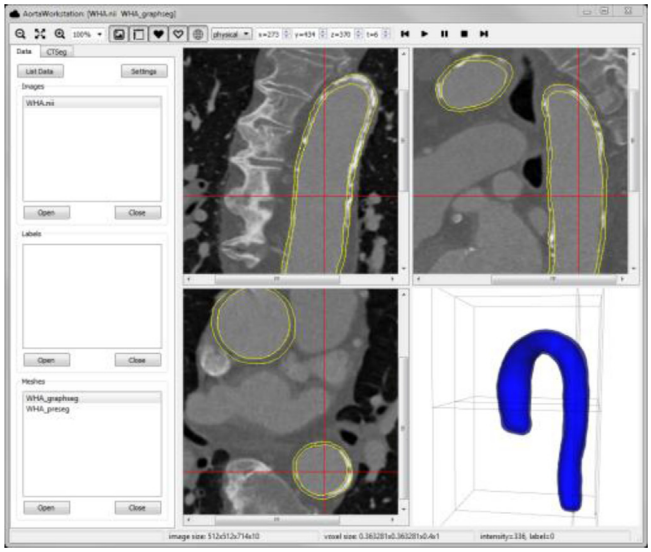

Figure 1 Example of data visualization: image data is shown on three orthogonal slices, segmented surface is shown by 3D rendering and its intersections with image slices (yellow contours).

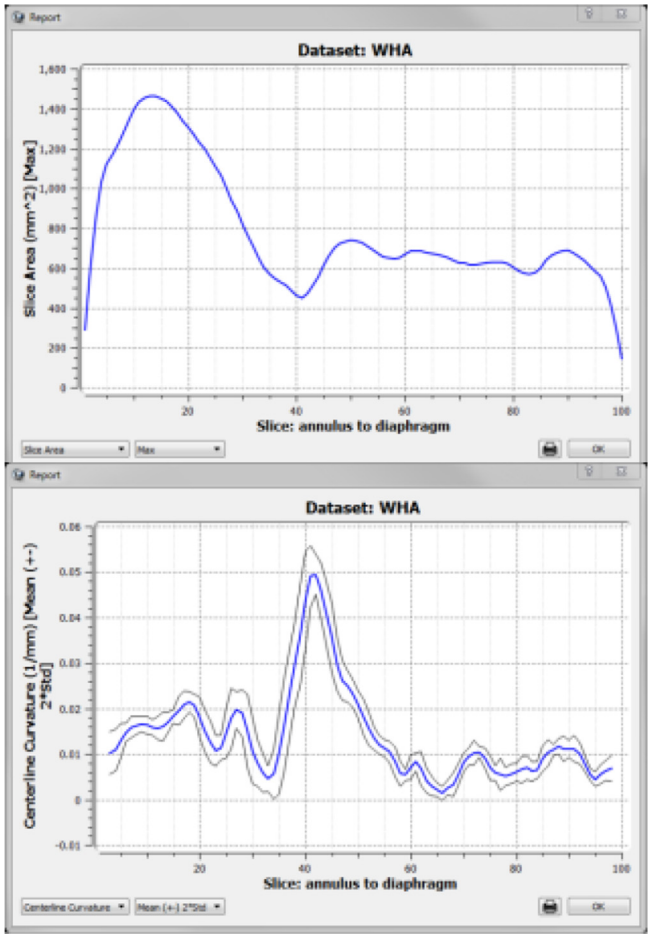

Figure 2 Examples of quantitative indices derived from a cardiac cycle. Top: maximal cross-sectional areas, bottom: range (mean and 2*standard deviation) of centerline curvature.

PO-11

SEX DIFFERENCES IN THE DEVELOPMENT OF ABNORMAL ENDOTHELIUM-DEPENDENT VASODILATION IN AORTA FROM TYPE 2 DIABETIC RATS: POSSIBLE ROLE OF NITRIC OXIDE

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Little is known about the interaction between diabetes and sex in vasculature. This study was designed to investigate whether there were sex differences in rat aortic endothelium-dependent vasodilation (EDV) in Zucker diabetic fatty (ZDF) rats, and the potential role of nitric oxide (NO). EDV to acetylcholine (ACh) was measured in aortic rings pre-contracted with phenylephrine (PE). Contractile responses to PE were generated before and after treatment with L-NAME (200 μM), a NO synthase (NOS) inhibitor. In addition, the levels of endothelial NOS (eNOS) and NADPH oxidase (NOS, a potent source of superoxide) mRNA expression were determined using real-time RT-PCR. Type 2 diabetes significantly impaired EDV in aortic rings from female ZDF rats, however, potentiated the relaxation in males. Diabetes decreased the contractile responses to PE in aortic rings from rats, regardless of sex. Moreover, diabetes enhanced the extent of PE potentiation after blocking eNOS with L-NAME in females. Accordingly, the levels of eNOS mRNA expression were substantially enhanced in aorta of female ZDF rats compared to those in lean animals. In addition, Nox1 and Nox4 mRNA expression were substantially enhanced in aorta of female ZDF rats. These data suggest that the predisposition of the female aorta to injury in type 2 diabetes may be, in part, due to the alteration of NO production (supported by NIH/NIDCR).

PO-12

RACIAL DIFFERENCES OF eNOS EXPRESSION RESPOND TO C-REACTIVE PROTEIN

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Background: African Americans (AA) have higher rates of cardiovascular diseases (CVD) compared to Caucasians (CA). Endothelial dysfunction is a common feature of CVD risk factors. Previous studies suggest racial differences in endothelial function exist at the physiological level. C-reactive protein (CRP), a risk marker for CVD, causes a reduction in eNOS expression and bioactivity in endothelial cells (ECs). AA individuals have significant higher concentrations of CRP than Caucasian (CA) individuals. The aim of this study was to investigate the racial differences of endothelial function under CRP stimulation at the cellular level.
Methods: Eight human umbilical vein endothelial cells (HUVECs) lines from African American (AA) and Caucasian (CA) donors with gender split evenly were cultured and incubated with CRP for 24-hrs. Doses of CRP were 0, 25, 50 and 100 μg/mL. Western blot was conducted to measure the expression of eNOS after CRP incubation. ImageJ densitometric analysis of eNOS bands expressed in relation to β-actin.