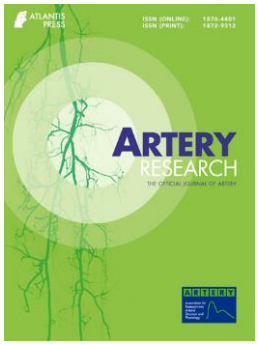

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# P8.11: ADIPOKINE DYSREGULATION IS ASSOCIATED WITH ARTERIAL STIFFNESS IN A MODEL OF DIET-INDUCED OBESITY IN MICE

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### P8.7
### PRESERVATION OF BIOMECHANICAL PROPERTIES OF ARTERIES IN EMBALMED BODIES

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Minimally invasive surgery techniques such as laparoscopic, endoscopic and thoracoscopic procedures became current practice and recently have revolutionized the specialty of vascular surgery. However, the practice and skills of surgeons are crucial to perform correctly the numerous highly sophisticated and delicate procedures of this surgical specialty. Normally for training are used simulators, which have a known limitations. Sometimes, there are also using very expensive and not always available fresh cadavers, due to the importance of biomechanical properties of arteries for the training.
The use of embalmed cadavers assumes the better results in the surgeon comprehension of complex anatomic and vascular exposures and can improves their operative confidence. However, a traditional formaldehyde-embalming method cannot preserve the structure and properties of the vascular system.
In order to remove these limitations we have developed a new embalming perfusion method aiming to satisfy the needs to support the embalmed bodies as true simulator for vascular surgery.
In this study, we present results of histological analysis and evaluation of mechanical properties of the arteries, achieved with our perfusion system, and its comparison with formaldehyde-embalming method. Other important features, such as the authenticity of colour, tissue consistency and elasticity (flexibility) of the vascular vessels, are also discussed.

### P8.8
### APELIN/APJ RECEPTOR SYSTEM INVOLVEMENT IN OBESITY-RELATED VASCULAR REACTIVITY CHANGES

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**Background:** Obesity associated changes of vascular reactivity could be related to inadequate secretion of adipokines. Apelin is an adipokine with cardiovascular, endocrine and metabolic actions. We aimed to investigate the possible modulator actions of apelin on obesity induced changes of vascular reactivity.
**Methods:** Obese prone (OP-CD) rats and obese resistant (OR-CD) rats were fed high-fat diets. After 4 weeks the pulmonary and mesenteric arteries were used to comparatively analyse the contractile (induced by phenylephrine - Phe) and relaxant (induced by acetylcholine ACh) responses. Localization of apelin and its APJ receptor was determined using immunohistochemistry.
**Results:** The Phe -induced contraction was amplified on PA and ACh -induced relaxation was reduced on both PA (with 62%) and MA (with almost a half) in OP-CD as compare with OR-CD. Pre-treatment with apelin 13 (AP13) improve ACh effect on PA rings form OP-CD. Administration of apelin-13(F13A) receptor antagonist increase the Emax of Phe MA from OP-CD (with 26%) and decreased the ACh effect on all rings from both OP-CD and OR-CD rats. IHC demonstrate a decrease of apelin on PA endothelium but no differences on MA for either AP or APJ receptor.
In **conclusion**, the apelin/APJ peptidergic system could be involved in obesity related reactivity alteration of arteries from both pulmonary and systemic circulation.

### P8.9
### MECHANICAL BEHAVIOR OF THE ABDOMINAL AORTIC ANEURYSM OBTAINED FROM THE RAT XENOGRAFT MODEL AND TREATED BY MESENCHYMAL STEM CELLS

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To prevent rupture of abdominal aortic aneurysms (AAAs), current preventive treatments involve surgery or the deployment of an endovascular stent. The development of gene or cell therapies as alternative therapeutics to stabilize AAAs represents a challenge. In the present contribution, we investigate the effect of a mesenchymal stem cell therapy on the mechanical properties of the rat xenograft model of AAA. This model reproduces the arterial dilation of the aneurismal disease and has been much used to study the biological impact of different approached therapies. The arterial structure of healthy native rat abdominal aortas, diseased untreated and treated AAAs were subjected to axial extension and pressurization tests (biaxial mechanical tests) in a pressure myograph device. A nonlinear hyperelastic and incompressible mechanical model was used to identify and compare the material parameters for the three specimen types. Histological analysis enabled a correlation between the results and the microstructure of the arterial tissue and particularly the presence of a thrombus or a neointima layer. Stress distributions within the arterial wall should then be computed by finite element modeling in order to predict the risk of rupture of aneurysms.

### P8.10
### VASCULAR CHARACTERIZATION BY MEANS OF WAVE INTENSITY ANALYSIS: A PRELIMINARY STUDY IN MICE

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Mouse models are increasingly employed in the comprehension of cardiovascular disease. Vascular characterization could be enriched with Wave Intensity Analysis (WIA), which provides additional information about the vascular system and its interaction with the heart. We investigated age-associated changes in vascular parameters of mice in different arterial sites and explored the role of WIA.
Five adult (5 months) and five old (16 months) wild type male mice (strain C57BL6) were examined. Instantaneous values of diameter and flow velocity were automatically achieved from carotid and abdominal aorta B-mode and PW-Doppler images and elaborated to provide the lnD-V loop; pulse wave velocity values (PWVcar and PWVabd) and relative distension measurements (relDcar and relDabd) were calculated for both carotid artery and abdominal aorta. The WIA, as introduced by Parker in 2009, was performed: the amplitudes of the first local maximum (W1_car and W1_abd) and minimum (Wb_car and Wb_abd) were calculated.
PWVcar (adult: 1.41±0.37, old: 2.19±0.49 m/s), PWVabd (1.89±0.63 vs 2.89±0.68 m/s), relDcar (27%±5.9% vs 19.7%±3.6%) and relDabd (26.2%±4.1%, vs 15.4%±3.6%) values were significantly different ($p<0.05$) in the two age groups. W1_abd amplitude was higher in adult than in old mice ($12.9\pm6.7\times10^{-7}$ $m^2/s$ vs $5.5\pm2.2\times10^{-7}$ $m^2/s$, $p<0.05$); the same trend was found in Wb_car amplitude ($9.07\pm4.8\times10^{-8}$ vs $4.27\pm1.24\times10^{-8}$ $m^2/s$), even if the difference was not significant ($p=0.09$).
The age-associated decrease in W1_abd may suggest a change in cardiac contractility, while that in Wb_car may be related to alterations in reflected waves from cerebral circulation. Therefore, WIA might provide additional information to standard vascular biomarkers.

### P8.11
### ADIPOKINE DYSREGULATION IS ASSOCIATED WITH ARTERIAL STIFFNESS IN A MODEL OF DIET-INDUCED OBESITY IN MICE

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The aim of this work was to analyze vascular remodeling and mechanical alterations in mesenteric arteries in a model of diet-induced obesity in mice, as well as the impact of adipokine dysregulation in those changes. Four-week old CB57BL/6J male mice were assigned either to a control (10% kcal from fat) or to a high-fat (HF) diet (45% kcal from fat). After 32 weeks of diet, HF animals weighed 30% more than controls ($p<0.001$). Moreover, HF animals exhibited an increase in leptin but a reduction in adiponectin plasma levels. Studies of arterial structure and mechanics, performed by pressure myography did not reveal a significant vascular remodeling in HF mice. However, we observed a significant increase in arterial stiffness in HF mice, as assessed by b-values (obtained from stress-strain relationship; LF=2.4±0.5 *vs* HF=5.3±0.8, $p<0.05$) and pulse wave velocity values (LF=3.4±0.1 *vs* HF=3.9±0.1; $p<0.05$). Moreover, though we did not find differences in elastin content, a significant reduction in fenestrae number with HF diet together with a significant increase in collagen I amount ($p<0.05$) were observed. Positive and negative correlations were found between b-values and leptin or adiponectin levels, respectively ($p<0.01$). In conclusion, these data demonstrate that HF diet accounts for an increase in arterial stiffness that is associated with adipokine dysregulation. Supported by grants from Ministerio de Ciencia e Investigación (BFU2011-25303), Ministerio de Economía y Competitividad (SAF2009-09714, SAF2011-25303, BFU2012-35353), Grupos Universidad Complutense de

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**P8.12**
**ARTERIAL DISTENSION-PRESSURE LOOP ANALYSIS IN HYPERTENSIVE RATS: ADVANTAGES, PITFALLS AND POSSIBILITIES**

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Arterial wall viscosity (AWV) of central arteries, as well as distensibility, is important to properly buffer systolic ejection pressure. AWV is measured either by the area within the hysteresis of distension-pressure (DD-P) loop, defined as the viscous energy (AWV=Ve) or the ratio of Ve/Ve+energy stored during systole (=AWV%). We record DD-P loop via echotracking; averaged over 30 cardiac cycles, AWV and AWV% are calculated via MatLab software. Here we perform a post analysis of the DD-P loop in 12 groups of rats (n=5-8): normo- or hypertensive, with and without arterial remodeling, at different operating blood pressures (BP), using different compounds. AWV decreases and DD-P loop is flattened with increased BP; moreover it is differently altered if pulse pressure (PP) is altered and remains low at any operating BP in models with vascular wall remodeling. However in all conditions the ratio AWV% is poorly modified. Our results suggest that the AWV as the Ve (hysteresis loop area) is the most relevant in defining the viscous properties of the artery; they indicate that mean operating BP, PP and structural distensibility independently participate in modifying the shape of the loop which is largely dependent on the delay between peak systolic pressure and peak systolic diameter, apparent in the higher BP of the loop. This suggests that isobaric distensibility cannot be compared in the lower and upper part of the loop but only at a similar mean BP. Further studies will aim to confirm these suggestions and determine how to improve loop hysteresis evaluation

**P8.13**
**A 1-D MODEL OF THE SYSTEMIC ARTERIAL TREE IN MICE**

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Cardiovascular diseases are often studied at a pre-clinical stage using dedicated mouse models. However, (non-)invasive measurements in the murine cardiovascular system are difficult to obtain, limited to a restricted number of aortic locations, and need to be justified from an ethical perspective. In this work we present a 1-D model of the systemic circulation in mice. Murine arterial tree dimensions have been acquired and averaged from the segmentation of Micro-Computed Tomography (μ-CT) scans of 3 wild-type C57Bl/6 mice (12-15 weeks old). The resulting geometry consists of 85 arterial segments, including all major aortic branches as well as the tail and the cerebral tree. The remaining input to the model has been obtained from a wide range of literature data. An empirical relationship has been fitted to estimate the local arterial wall distensibility in all segments. Peripheral vessels are terminated with three-element windkessel models to account for the resistance and compliance of the distal vasculature. The integrated form of the momentum and continuity equations is solved numerically to yield pressures and flows throughout the arterial network. The model predicts pressure and velocity waveforms in good qualitative and semi-quantitative agreement with invasive pressure measurements as well as high-frequency ultrasound Pulsed-Wave Doppler aortic velocity and M-mode aortic distensibility measurements. In conclusion, a well-tuned and appropriately validated 1-D model for the murine cardiovascular system has been developed, which is ready to serve as a versatile study tool in the field of pre-clinical cardiovascular research.

**P9.1**
**INFLUENCE OF INSULIN SENSITIVITY AND RELATED METABOLIC FEATURES ON CAROTID AND AORTIC STIFFNESS IN NORMAL SUBJECTS**

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Insulin resistance (IR) underlies a cluster of metabolic abnormalities contributing to atherosclerosis. Relations between IR and large artery involvement in subjects without atherosclerotic disease are still debated.

**Aim**: to investigate in normal subjects the relations between IR and its associated metabolic abnormalities with tissue biomarkers of preclinical vascular involvement.
**Methods**: Eighty-two healthy volunteers (45 men; age 46±9) underwent a glucose tolerance test and a euglycemic hyperinsulinemic clamp to estimate IS (M/I, i.e. M value normalized by FFM and mean plasma insulin). Metabolic parameters measured included fasting and 2-hour glucose and insulin, detailed lipid profile, leptin, adiponectin and hs-CRP. Vascular examination included carotid-femoral pulse wave velocity (PWV) and radiofrequency-based ultrasound (QIMT® and QAS®, Esaote), for IMT and local stiffness estimate (beta index, BI). Acoustic properties of carotid wall were evaluated by videodensitometry and described as mean grey levels (MGL).
**Results**: in multiple regression models adjusted for sex and smoking, IMT was independently related directly to age and carotid diameter, and inversely to adiponectin (R2=0.34), IMTmax to age, systolic BP and adiponectin (R2=0.35), and carotid MGL to age and adiponectin (directly and inversely, respectively; R2=0.30). BI was related to age and M/I (directly and inversely, respectively; R2=0.44) and carotid-femoral PWV to age and glucose (directly; R2=0.39).
**Conclusions**: metabolic factors related to IR influence structure and function of carotid artery behind the main role of age. Adiponectin has an independent effect on carotid structure, while IS and plasma glucose mainly influence carotid and aortic stiffness.

**P9.2**
**VASCULAR ADAPTATIONS TO BODY SIZE AND COMPOSITION IN ADOLESCENTS**

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**Background**: increase in body mass index is accompanied by metabolic alterations but also by increased stroke volume (SV). Therefore, associated changes in vascular structure and function can not reflect only preclinical atherosclerosis but physiologic adaptation to body composition-related hemodynamic changes.
To evaluate the relationships between body composition and arterial structure and function without the influence of atherosclerotic risk factors, we assessed carotid intima-media thickness (IMT), luminal diameter (LD), wave speed (WS) and local pulse pressure (cPP)by radio-frequency based ultrasound (QIMT® and QAS®, Esaote), in 80 healthy children-adolescents with wide range of age (8-16 years) and BMI (15-40 kg/m2). Body composition was assessed by bioimpedance, visceral fat (VF) by ultrasound, and SV by Doppler. Plasma lipids, glucose and insulin were determined.
**Results**: body weight (BW) and fat free mass (FFM) were related to IMT (r=0.61 and 0.50), LD (r=0.54 and 0.53), WS (r=0.43 and 0.56) and cPP (r=0.36 and 0.49); fat mass (FM) was related to IMT and LD (r=0.40 and 0.29), and VF to IMT (r=0.41). SV was more strongly related to FFM than to FM (r=0.70 and 0.24). In multivariate models, IMT was determined by BW and triglycerides (R2=0.44), LD by BW and male sex (R2=0.37), WS by FFM and systolic BP (R2=0.39), cPP by FFM (R2=0.24). When SV was included into the models, it replaced FFM in model of cPP. Conclusion: adiposity-related changes in carotid function are depending on FFM-related increase in SV. Changes in carotid geometry also reflect an increase in body fat and plasma lipids.

**P9.3**
**LOWER SUBENDOCARDIAL VIABILITY RATIO IN DIABETIC WOMEN—CONTRIBUTING TO THE ABROGATED CARDIOPROTECTIVE EFFECT OF FEMALE GENDER IN DIABETES?**

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The cardioprotective effect of female gender is abrogated in the presence of type 2 diabetes, and female diabetic patients thus face comparable cardiovascular risk as men with type 2 diabetes. The SubEndocardial Viability Ratio (SEVR) is an index of myocardial oxygen supply and demand that can be assessed non-invasively by applanation tonometry. We hypothesized that diabetic women would have lower SEVR than diabetic men and non-diabetic subjects independently of conventional risk markers and arterial stiffness.