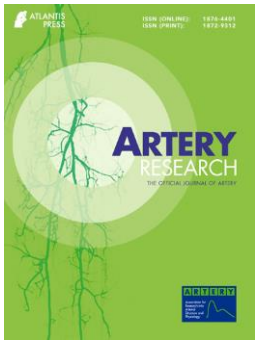

**Artery Research**

**ISSN (Online): 1876-4401 ISSN (Print): 1872-9312**
**Journal Home Page: https://www.atlantis-press.com/journals/artres**

# P3: UNDERSTANDING THE ENDOTHELIAL – SMOOTH MUSCLE – FIBROBLASTIC CELLS INTERACTIONS ON A TISSUE-ENGINEERED VASCULAR GRAFT

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**To cite this article**: Tatiana Felizardo, Nuno M. Neves, Albino Martins, Rui L. Reis (2018) P3: UNDERSTANDING THE ENDOTHELIAL – SMOOTH MUSCLE – FIBROBLASTIC CELLS INTERACTIONS ON A TISSUE-ENGINEERED VASCULAR GRAFT, Artery Research 24:C, 80–81, DOI: https://doi.org/10.1016/j.artres.2018.10.056

**To link to this article**: https://doi.org/10.1016/j.artres.2018.10.056

Published online: 7 December 2019

Artery Research (2018) 24, 80–132

Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.elsevier.com/locate/artres

# ARTERY 18 Poster Session

## Poster Session I – Basic

### P1
### DETERMINANTS OF PERIPHERAL PULSE PRESSURE AND PULSE PRESSURE AMPLIFICATION

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**Objective:** Peripheral (e.g. brachial) Pulse Pressure (Ppp) exceeds central pulse pressure (Cpp) corresponding to the first (Cpp1) or second (Cpp2) peaks in the central waveform. This pulse pressure amplification, attributed to propagation of the pulse wave from aorta to periphery and influence of reflection in the periphery, is measured as Ppp/Cpp2 (when Cpp2 > Cpp1). We examined whether the haemodynamic determinant of Ppp relates more closely to Cpp1 rather than Cpp2.
**Methods:** We examined the theoretical influence of change in morphology of central aortic waveform on peripheral waveform when applying a reverse transfer function to the aortic waveform. Secondly, we examined the relationship between central and peripheral waveforms during modulation of central pressure with nitroglycerine (GTN). Central pressures were obtained during cardiac atheterization with a Millar catheter placed in the proximal aortic root in patients with non-critical coronary artery disease (n = 15) at baseline and after GTN. The digital arterial pulse was acquired simultaneously with a servo-controlled finger cuff.
**Results:** In theoretical analysis, Ppp was sensitive only to the portion of the waveform up to the time of Cpp1. Similar results were observed with GTN, which had no significant effect on Cpp1 (38.7 ± 2.0 and 37.1 ± 2.5 mmHg at baseline and after GTN respectively, P = 0.36) nor on Ppp (70.2 ± 5.0 and 69.2 ± 4.7 mmHg at baseline and after GTN respectively, P = 0.47) but reduced Cpp2 by 17.0 ± 1.8 mmHg (P < 0.001).
**Conclusions:** These results suggest that peripheral pulse pressure is determined by the early systolic portion of the central aortic pressure waveform up to the time of Cpp1 and may be independent of Cpp2.

### P2
### DETERMINATION OF LOCAL PULSE WAVE VELOCITY DOES NOT AFFECTED BY REFLECTION

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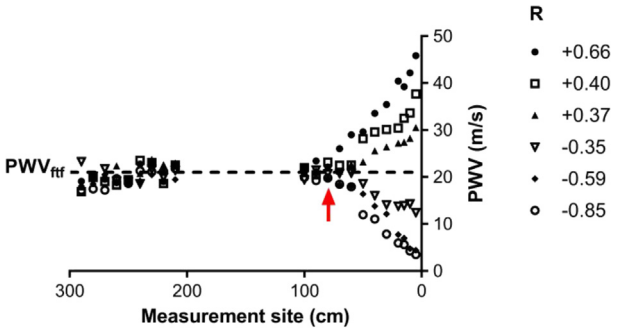
**Objective:** PWV is an important indicator of arterial stiffness and cardiovascular diseases. Local PWV would provide a more accurate estimation of local stiffness than does regional PWV. Local PWV is commonly determined by loop techniques, such as the PU-loop method and the aim of this study is to examine the effect of reflections on the accuracy of determining local PWV by loop Methods.
**Methods:** Pressure and flow were measured along a flexible tube that was connected to three positive and three negative reflections. PWV was calculated using the PU-loop method and wave intensity analysis was used to separate the pressure and flow velocity waveforms, using PWV of 20.2 m/s measured determined by the foot-to-foot method. Local reflection coefficient I was calculated as the ratio of magnitudes of backward to forward pressure.
**Results:** Figure 1 shows local PWV is not affected by the reflection until measurements were taken at 80 cm away from reflection site, when it starts to increase or decrease depending on the type of the reflection. The threshold of R corresponding to the non-affected PWV by reflections is ±0.36 ± 0.05 (mean ± SD).
**Conclusions:** The results of this study indicate that local PWV determined by PU-loop are only affected by reflections when the local reflection coefficient is greater than ±0.36 ± 0.05, irrespective of the distance to the reflection site. If/given reflections of the current study are comparable to those measured in vivo, PWV would not be affected by reflections in the arterial system.




| | R | | | | | |
|---|---|---|---|---|---|---|
| Distance from reflection | A | B | C | D | E | F |
| 5 (cm) | 0.66 | 0.40 | 0.37 | -0.35 | -0.59 | -0.85 |
| 80 (cm) | 0.40 | 0.32 | 0.24 | -0.15 | -0.45 | -0.60 |

### P3
### UNDERSTANDING THE ENDOTHELIAL – SMOOTH MUSCLE – FIBROBLASTIC CELLS INTERACTIONS ON A TISSUE-ENGINEERED VASCULAR GRAFT

Tatiana Felizardo, Nuno M. Neves, Albino Martins, Rui L. Reis
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There is still a pressing need to develop small-diameter vascular vessels for vascular reconstructive procedures. Tissue Engineering offers the prospect of being able to meet this medical demand, as it allows the development of structurally complex blood vessels substitutes 1. Accordingly, the ultimate aim of this work is to develop small diameter vascular substitutes based on layering multiple cell types. Co-culture systems of human endothelial-smooth muscle cells and fibroblastic-smooth muscle cells were initially established. These co-cultures were then assembled to develop a tri-culture system, which mimics the structural organization of a blood vessel. Electrospun nanofibrous meshes were

used as culturing substrates, which restrict cell migration although enabling biochemical communication 2. All the established culture systems presented viable and proliferive cell populations over time. Interestingly, the tri-culture system presented protein synthesis values much higher than the co-cultures, mostly of collagen. On the immunofluorescence micrographs were observed the maintenance of cell type-specific proteins expression, even in the presence of another cell type. Quantification of Growth Factors (GFs) on conditioned media of the co- and tri-culture systems demonstrated a synergistic interplay between Vascular Endothelial GF (VEGF) and basic Fibroblast GF (Bfgf). The VEGF was mainly expressed by smooth muscle cells, which leads to increasing levels in the co- and tri-culture systems. A similar trend is observed for Bfgf, expectedly produced by the fibroblastic cells. By its side, the platelet derived GF levels remain unaltered among conditions. This study demonstrated the fundamental importance of the intercellular crosstalk between endothelial, smooth muscle and fibroblastic cells. It reinforces the potential of a tri-culture system in the development of tissue engineered blood vessel substitutes.

**References**

1. Benrashid E, McCoy CC, Youngwirth LM, Kim J, Manson RJ, Otto JC, et al. Tissue engineered vascular grafts: Origins, development, and current strategies for clinical application. Methods: [Internet]. 2016;99:13—9. Available from: https://doi.org/10.1016/j.ymeth.2015.07.014
2. Martins A, Alves da Silva M, Reis RL, Neves NM. Polymeric mesh with selective permeability, for the repair and regeneration of tissues. WO/2014/016816 A1, EP 2878314 B1, US 2016/0038645 A1.

## P4

## MECHANISM OF PROANGIOGENIC ACTIVITY OF MITOCORRECTIN ON ENDOTHELIAL CELLS IN VITRO

Tetiana Nikolaienko, Victoriia Nikulina, Liudmyla Garmanchuk, Oleksander Makarenko
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**Background:** Investigations of different effective treatment modalities of infectious and inflammatory complications of stroke remain relevant. Normalization of vascularization, impaired due to hypoxia, is an important component of ischemic disease treating. The aim of our work was to study the mechanism of action of mitocorrectin on endothelial cells in vitro.
**Methods:** Active ingredient of mitocorrectin is a set of oligopeptides and amino acids isolated from cell mitochondria of the liver, brain and the pancreas (10:10:1) of pigs. As an experimental model was used endothelial cell line (PAEC), which was incubated at the standard conditions. Cytotoxic/proliferative effect on cultured cells was determined using cytofluorymetric analysis and MTT-test.
**Results:** Our studies have shown that mitocorrectin increased of endothelial cell by 25% and decreased apoptotic cells almost 2 times compared with the control. Cytofluorymetric analysis revealed an increase 1.8-fold in the population of proliferative cells pool under the influence of mitocorrectin. The most pronounced mitogenic and antiapoptotic effect of mitocorrectin on the endothelial cells was at concentrations of 0.1 — 1/ml. Thus, these doses may be the most therapeutically effective in restoring vascularization in post-stroke period. In addition, long-term cultivation of cells in the 2D-culture when exposed to mitocorrectin, more intensive formation of the capillary-like structures compared with controls, which may indicate vascular morphogenesis.
**Conclusions:** Thus, a study suggests that mitocorrectin shows a positive proangiogenic effect on endothelial cell line and this drug can be quite effective to restore vascularization, which is important in post-stroke period at ischemic complications.

## P5

## REGIONAL VARIATIONS IN THE MICROMECHANICAL AND BIOCHEMICAL PROPERTIES OF THE OVINE AORTA

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**Background:** It is important to understand regional variations in the mechanical and biochemical properties of the aorta to better predict and treat diseases. Although previous studies have been explored regional differences in the structure and biomechanical properties of the aorta, little is known about how these properties vary across its entire length [1, 2].
**Objectives:** To map the micromechanical and biochemical properties of the ovine aorta from the aortic root to the celiac artery region.
**Methods:** Fresh ovine aortas (n = 3) were split into nine sections, separated by 2 cm intervals between the aortic root and the celiac artery region. For each section, three biopsies were cut out using a 5 mm biopsy punch (a total of 81 biopsies). An oscillatory nanoindentation method was used to determine the micromechanical properties of the tissue [3]. 16 indents were made per biopsy. The shear storage (G'), the shear loss modulus (G'') were determined [3]. Subsequently, the same samples were used to determine elastin, collagen and glycosaminoglycan (GAG) levels using established biochemical assays.
**Results:** Overall, there was a significant correlation between an increase in G' and collagen ($P = 0.01$) with distance from the aortic root whilst elastin ($P = 0.05$) and GAG ($P = 0.05$) levels were significantly decreased.
**Conclusions:** Our study is the first to comprehensively map the mechanical and biochemical properties across the entire aorta. There was a progressive increase in mechanical properties from the proximal to the distal region, along with an increase in collagen and a decrease in elastin content.

**References**

1. Haskett D, Johnson G, Zhou A, Utzinger U, Geest JV. Microstructural and biomechanical alterations of the human aorta as a function of age and location. Biomechanics and modeling in mechanobiology. 2010 Dec 1;9(6):725-36.
2. Harkness ML, Harkness RD, McDonald DA. The collagen and elastin content of the arterial wall in the dog. Proc. R. Soc. Lond. B. 1957 Jun 25;146(925):541-51.
3. Akhtar R, Draper ER, Adams DJ, Hay J. Oscillatory nanoindentation of highly compliant hydrogels: A critical comparative analysis with rheometry. Journal of Materials Research. 2018 Apr; 33(8):873-83.

## P6

## ARTERIAL STRUCTURE AND COAGULATION IN AGEING NAKED MOLE RATS

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Vascular stiffening and a prothrombotic state consistently increase with age. Naked mole rats (NMRs) among rodent species have a maximum lifespan exceeding 30 years. Arterial stiffness assessed by pulse wave velocity and arterial pressure have been shown not to increase with age in NMRs (Grimes et al. AJP). The objective of this work was to study the relation between functional and structural arterial changes and plasma thrombin generation changes in young (2-year-old) and adult (9-year-old) NMRs. Collagen and elastin contents, vascular smooth muscle cell density and intimal thickening have been analyzed in the thoracic aorta, whereas plasma thrombin generation was assessed by calibrated automated thrombography associated with dosage of coagulation factors and endothelial markers.Our results showed no difference in collagen, elastin and vascular smooth muscle cell (VSMC) content between 2 (n = 5) and 9-year-old (n = 5) NMRs. There was no elastin degradation nor intimal thickening in NMRs at 9-years-old compared to 2-years-old. We showed no increase in plasma thrombin generation up to 9 years of age and no change in coagulant fibrinogen and factor VIII both known to increase normally with age. The expression of Endothelial Protein C Receptor (EPCR) and Thrombomodulin were similar at both ages.
In conclusion, young and adult NMRs do not show structural changes of the vascular wall in accordance with the absence of arterial stiffening. The conservation of an intact structure of the vascular wall and no change in endothelial markers during the first third of lifetime is compatible with the lack of a prothrombotic state.

## P7

## TELOMERE LENGTH AND AORTIC VALVE CALCIFICATION

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**Background:** Short telomere length (TL) is associated with atherosclerosis development. Aortic valve stenosis, an age-related disease characterized by narrowing of the aortic opening, is mainly caused by aortic valve