

Oral Session IV – Models, Methodologies and Interventions

Chair: J Baulmann, S Wassertheurer

Probing arterial stiffness at the nano-scale using the internal mammary artery as a novel target

Dr Riaz Akhtar

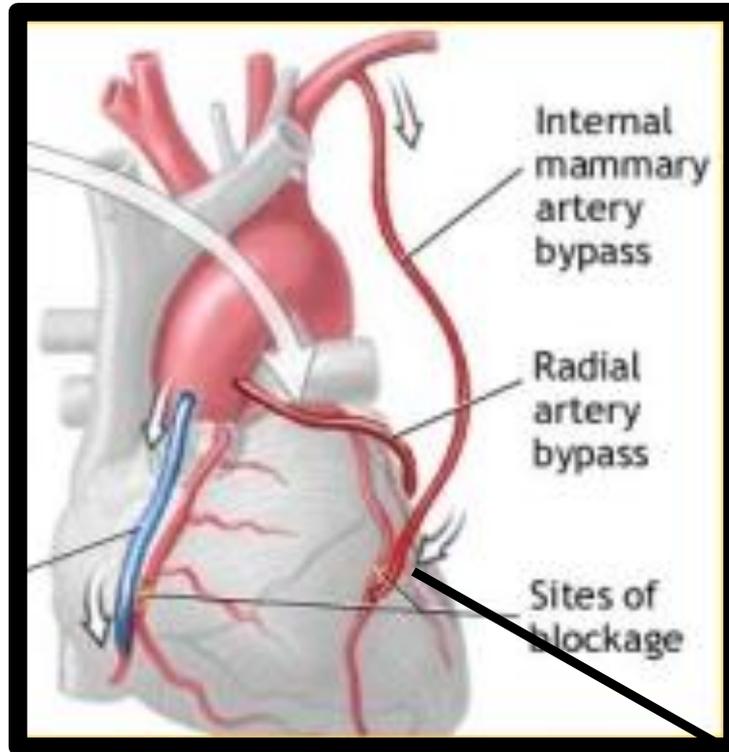
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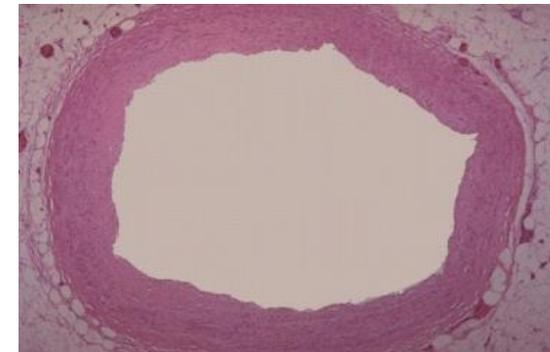
Internal Mammary Artery

Internal mammary artery serves as a model artery - reflects alterations in coronary and carotid arteries.



Extra part of the repair artery (CABG)
- nonatherosclerotic

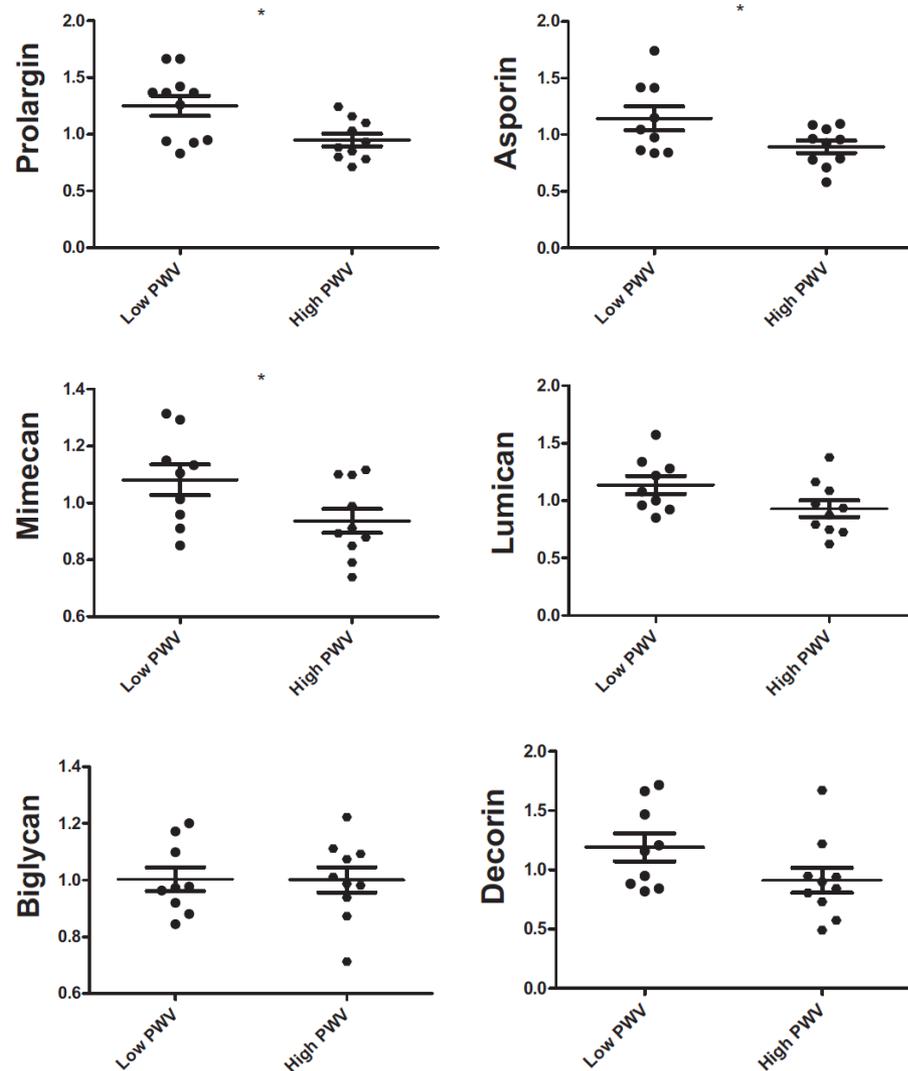
Internal mammary artery (IMA)



Arterial Stiffening and IMA

- Changes in the amounts of small leucine-rich proteoglycans (SLRPs) found in patients with high carotid-femoral PWV.
 - Downregulated in high PWV group.

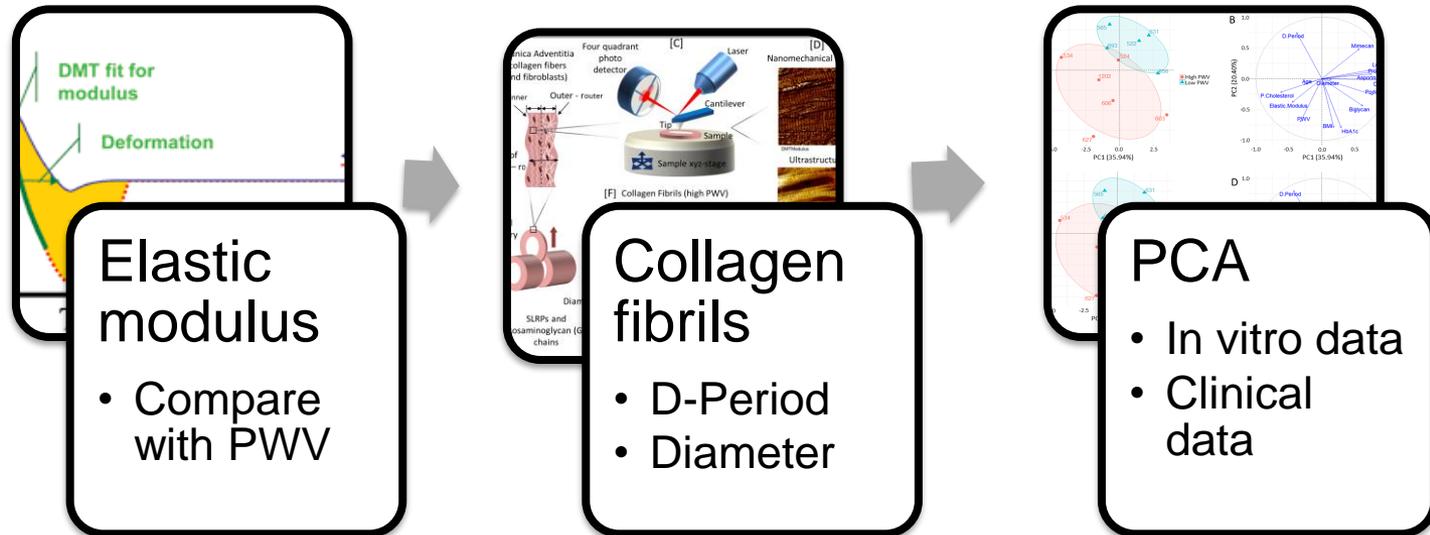
Prolargin
Asporin
Mimecan
Lumican
Biglycan
Decorin
Podocan



Hansen et al., Arterioscler Thromb Vasc Biol. (2015)

Aims

To determine whether nano-scale alterations in the IMA are manifested in patients with a high degree of arterial stiffening.

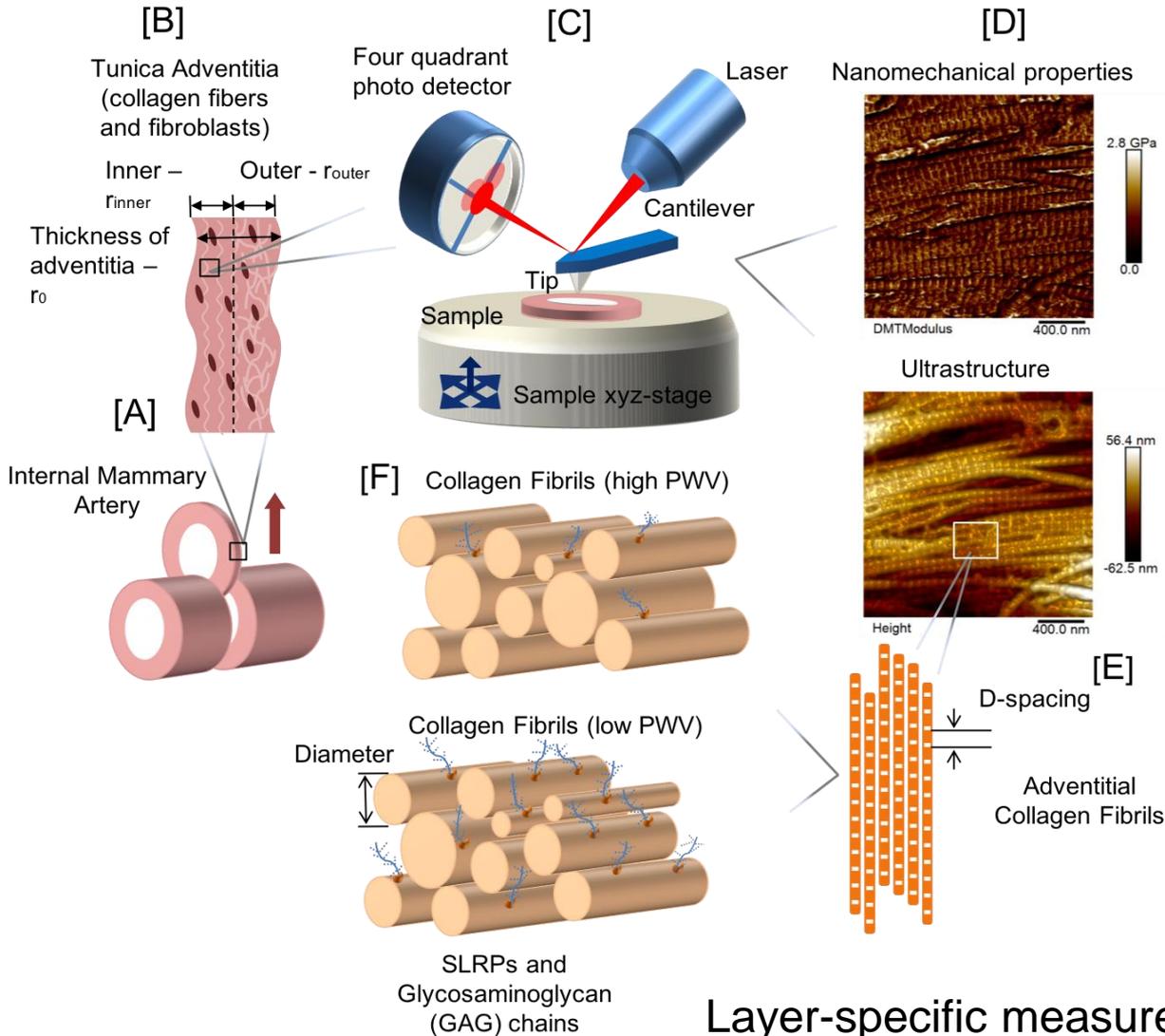


Low and High PWV Groups

IMA specimens were grouped into high PWV (13.4 ± 3 m/s, n=9) and low (8.6 ± 0.7 m/s, n=8)

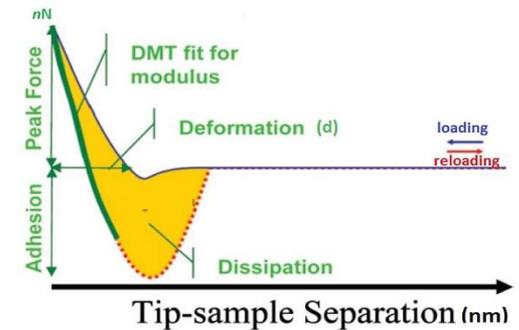
Clinical parameters	Low PWV		High PWV		P Value
	Mean	SD	Mean	SD	
Age, y	67.9	10.7	69.9	7	NS
BMI	26.5	4.7	28.4	4.6	NS
PWV, ms ⁻¹	8.5	0.7	13.4	3	<0.001
Systolic blood pressure, mm Hg	131.3	18.7	154.1	28.6	NS
Diastolic blood pressure, mm Hg	77	10.7	79.4	12.3	NS
Male, sex, %	87.5		100		NS
Diabetes, %	12.5		0		NS
Hypertension, %	50		66.7		NS
Smoking, %	62.5		88.9		NS
Total cholesterol, mmolL ⁻¹	4.1	0.5	4.9	1.5	NS
P-Cholesterol LDL, mmolL ⁻¹	2.1	0.5	3.1	1.3	NS
P-Cholesterol HDL, mmolL ⁻¹	1.2	0.1	1.1	0.3	NS
P-Triglyceride, mmolL ⁻¹	1.6	0.6	1.6	0.5	NS
P-creatinin, mmolL ⁻¹	89.8	19.9	91.6	20.4	NS
HbA1c (glycated haemoglobin (A1c))	0.06	0.007	0.06	0.002	NS

Experimental Approach



Peakforce QNM Method:
Derjaguin-Muller-Toporov (*DMT*)
model

$$E = \frac{3(F_{tip} - F_{adh})}{4\sqrt{R} d^3}$$



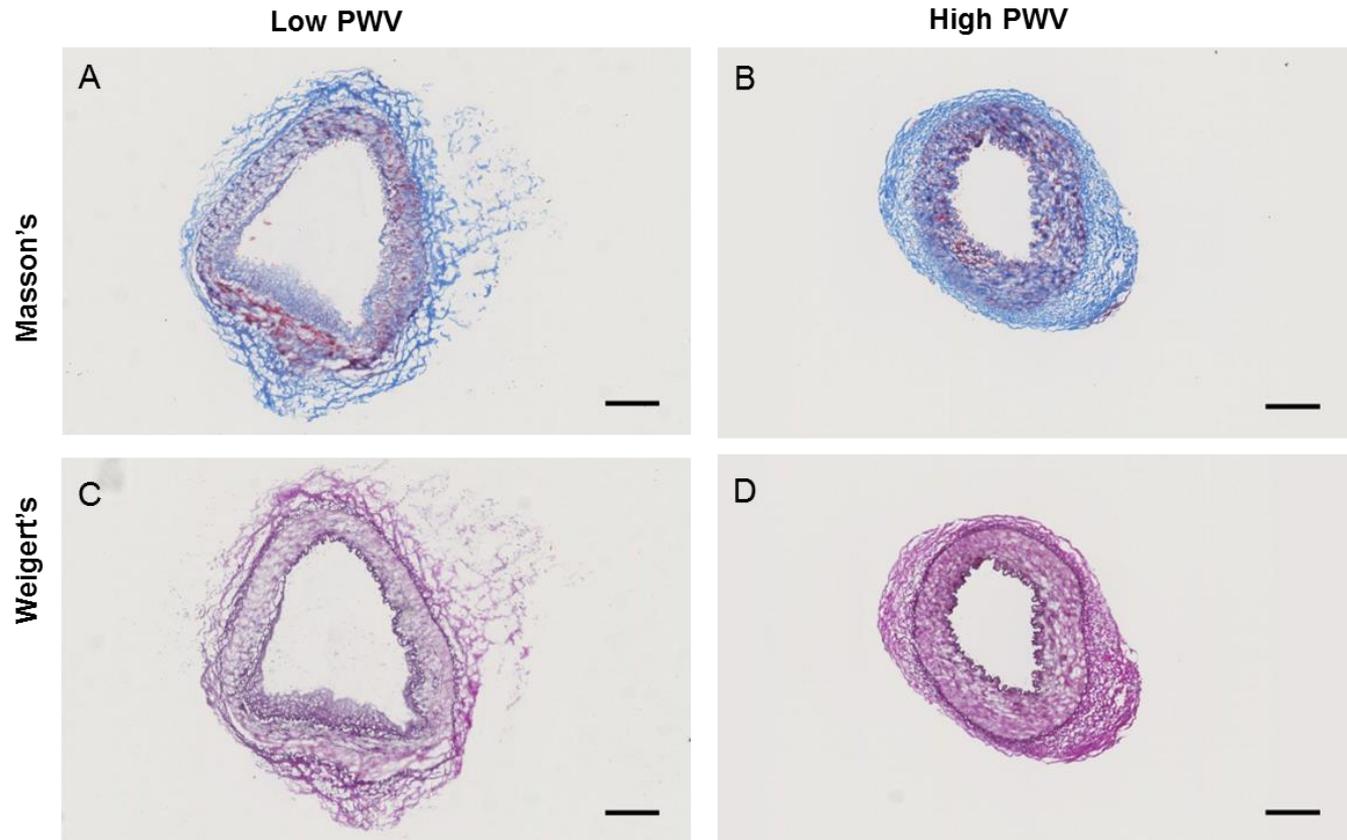
Papi et al. Applied Physics Letters (2014)

Layer-specific measurements: Adventitia and Media

Transition Artery

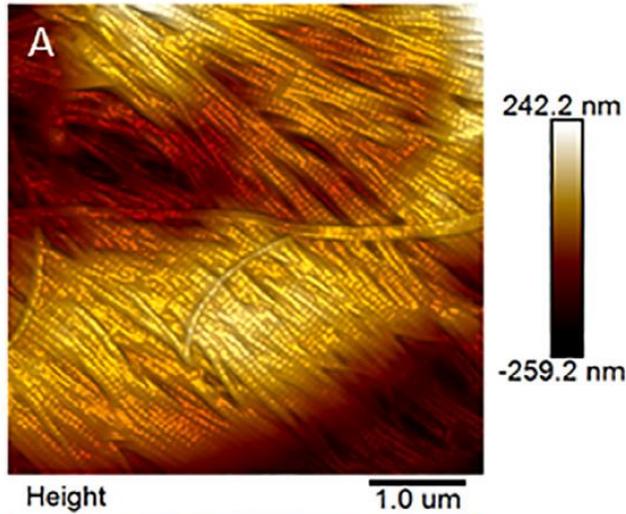
Intima-media
thickness:

- $162.10 \pm 78.3 \mu\text{m}$
(low PWV)
- $209.3 \pm 76.6 \mu\text{m}$
(high PWV)
- $p = 0.19$.

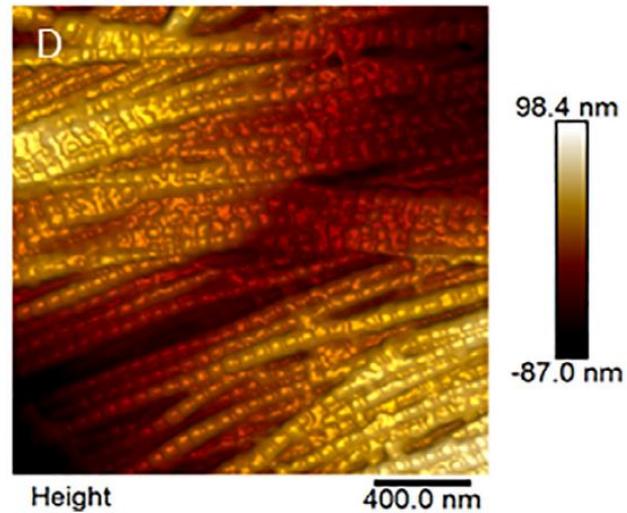
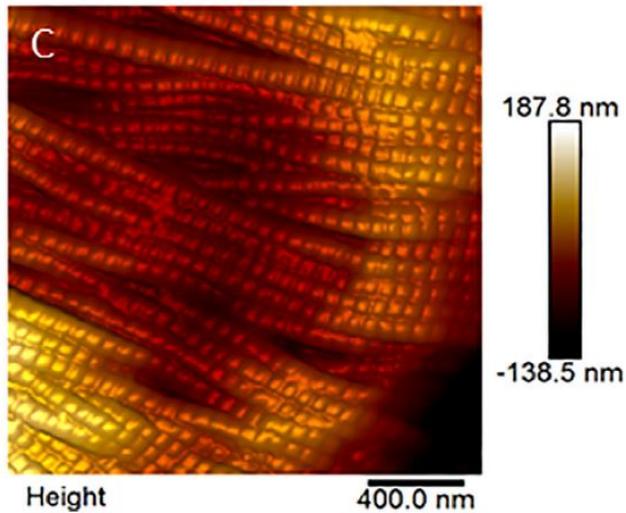
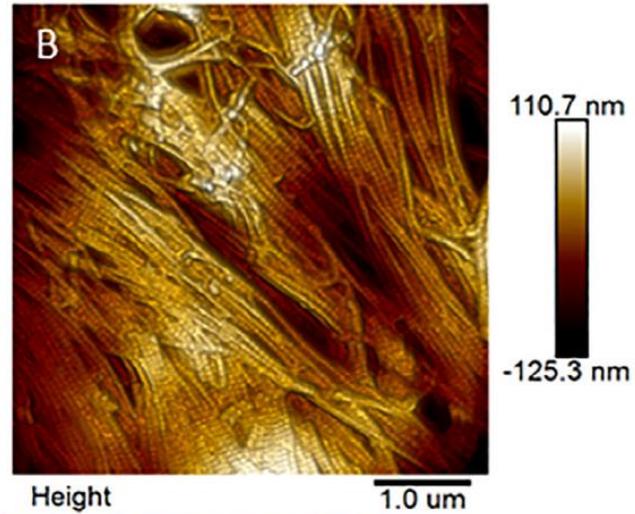


Adventitial Collagen Fibrils

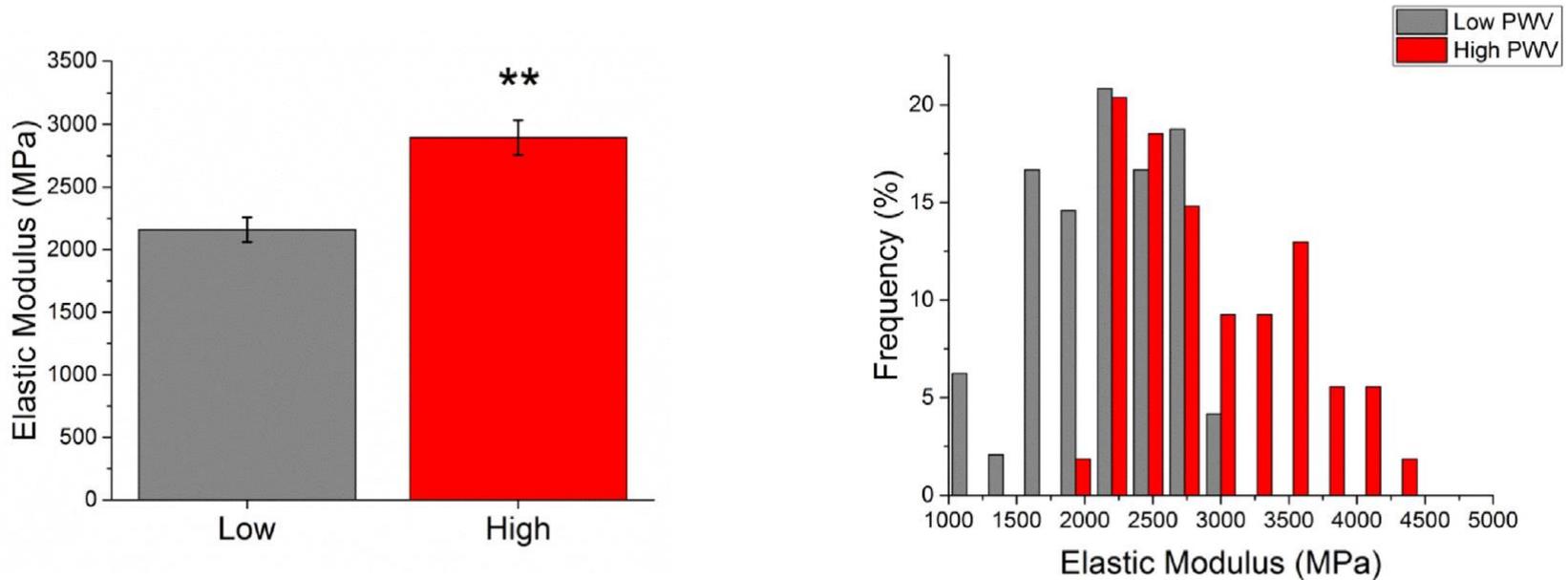
Low PWV



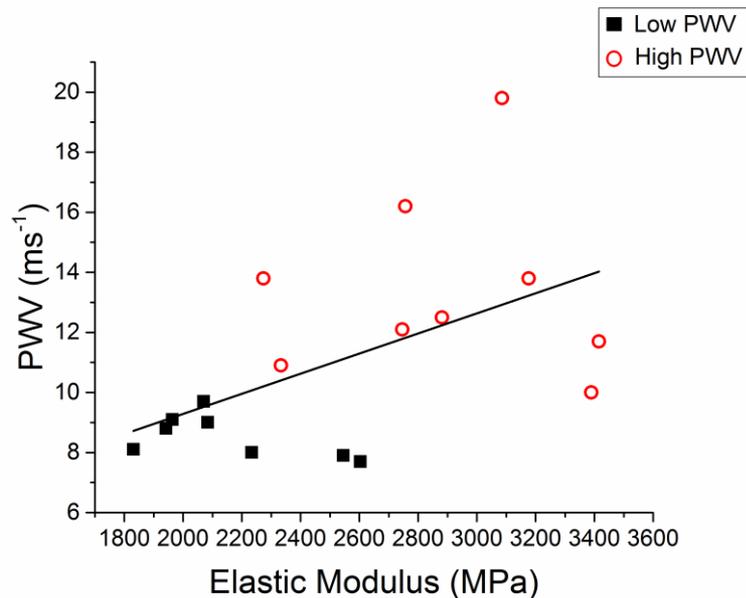
High PWV



Nanomechanical Properties and PWV



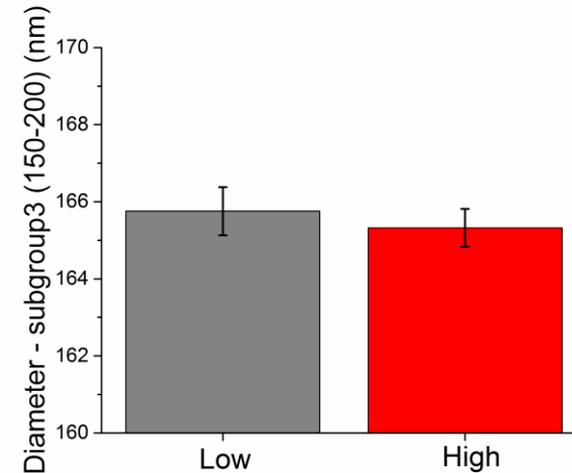
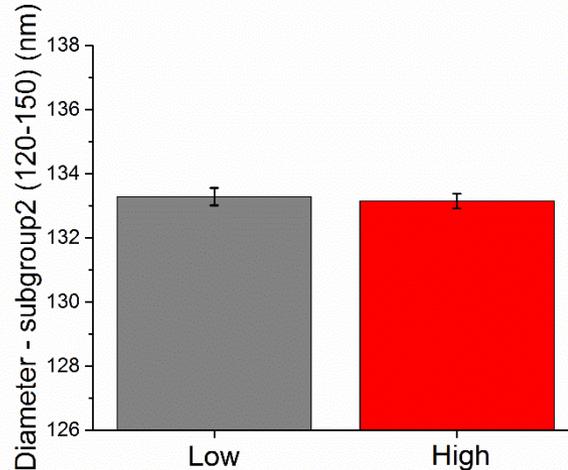
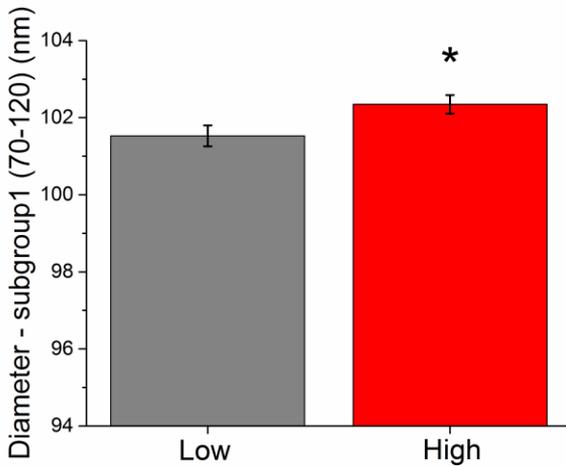
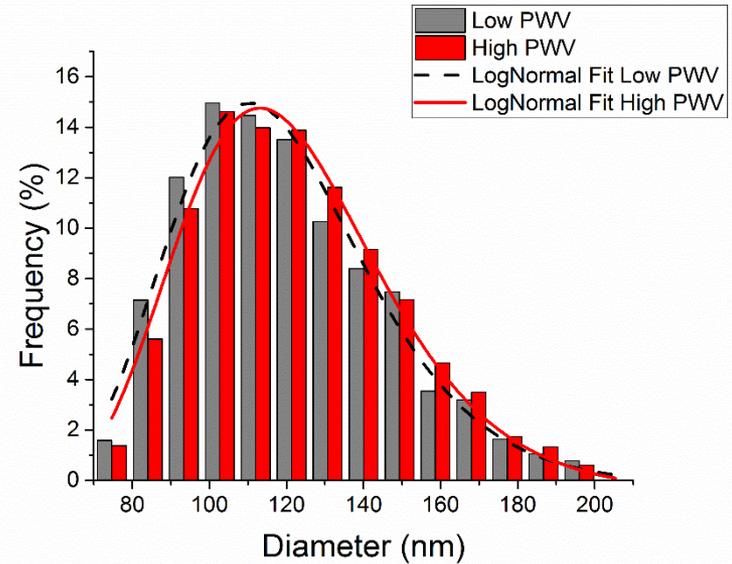
Spearman's Rank Order Correlation, $\rho = 0.02$



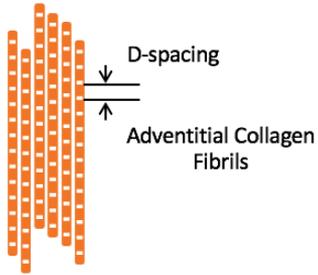
Collagen Fibril Diameter

Statistically significant difference in distribution:

- 70-120 nm sub-group

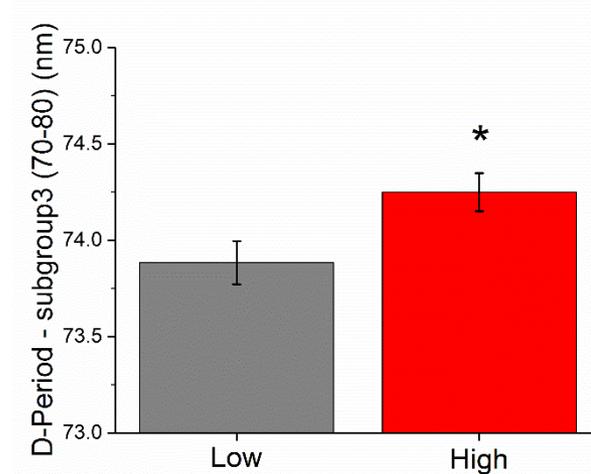
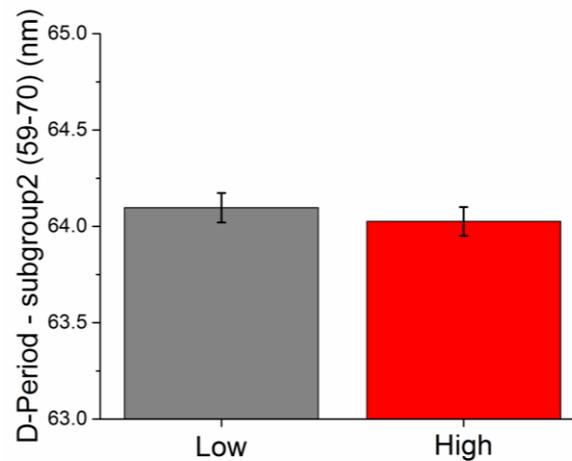
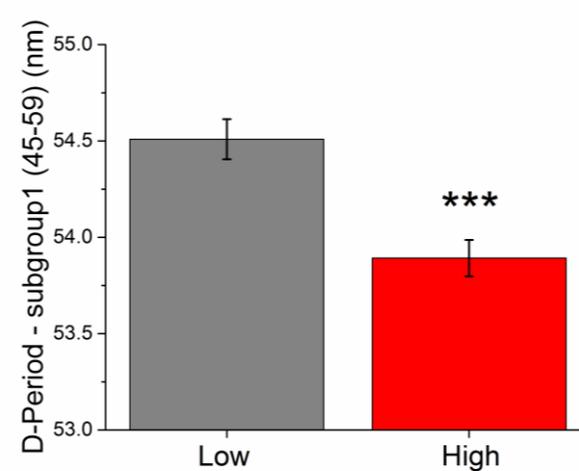
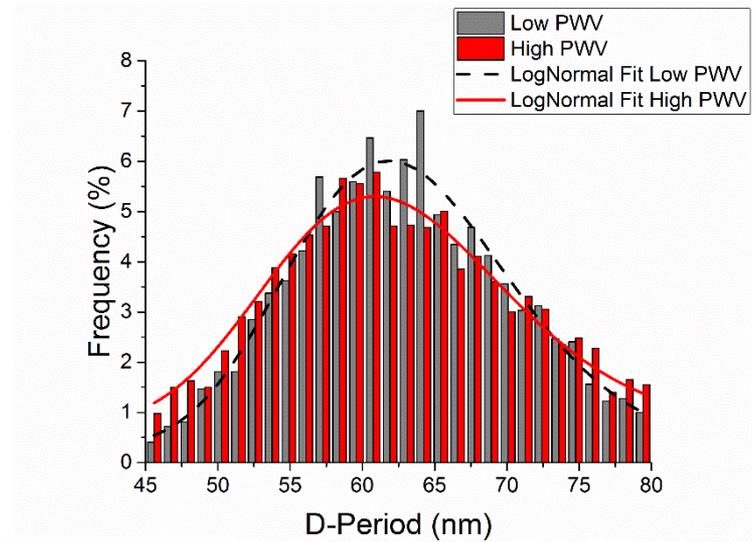


Collagen Fibril D-Period



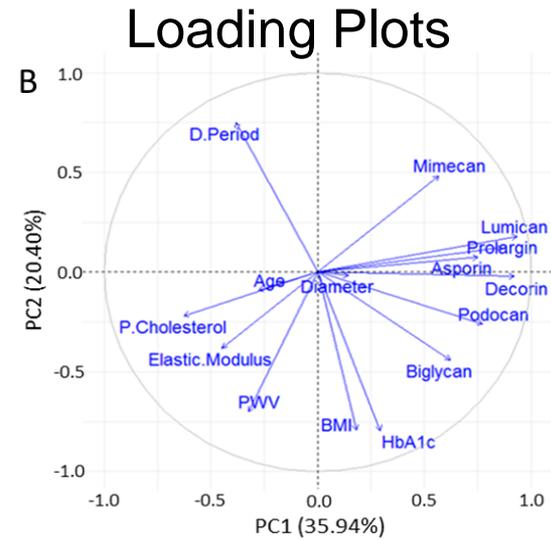
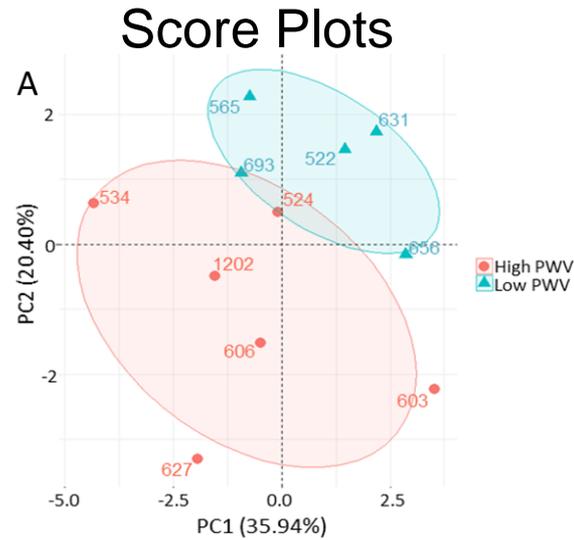
Statistically significant difference in distribution:

- 45-59 nm sub-group
- 70-80 nm sub-group

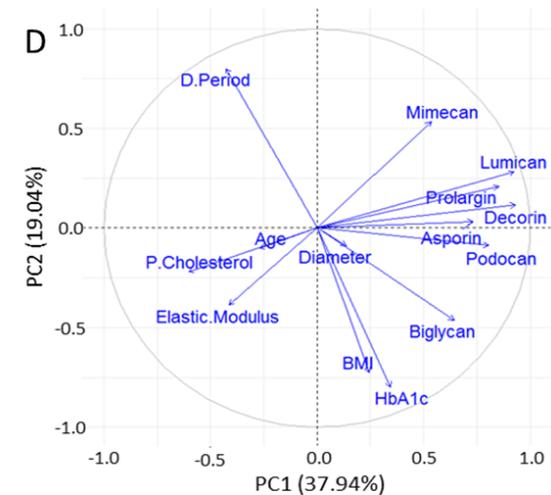
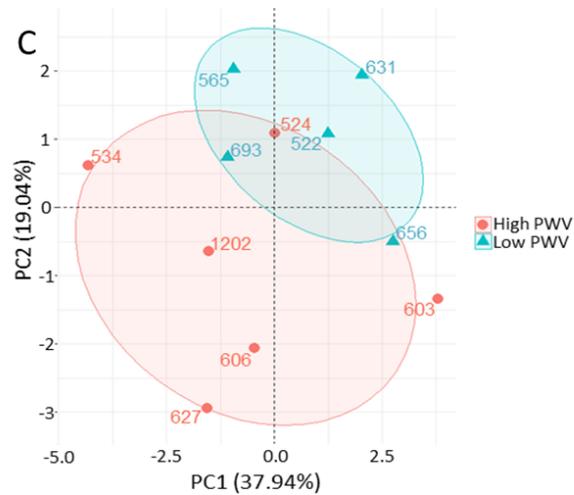


PCA Analysis - Separation with Nanomechanical Properties

PWV and Elastic modulus



Elastic modulus only

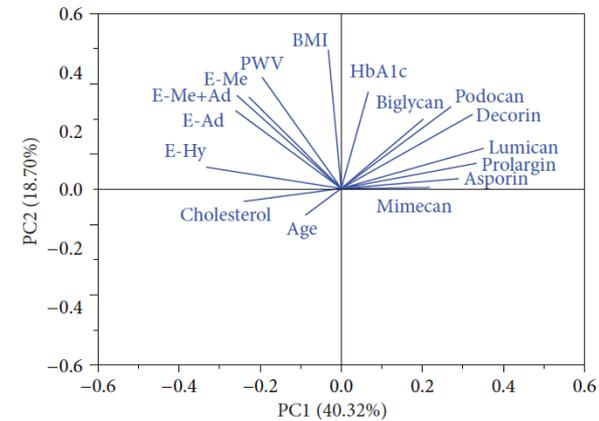
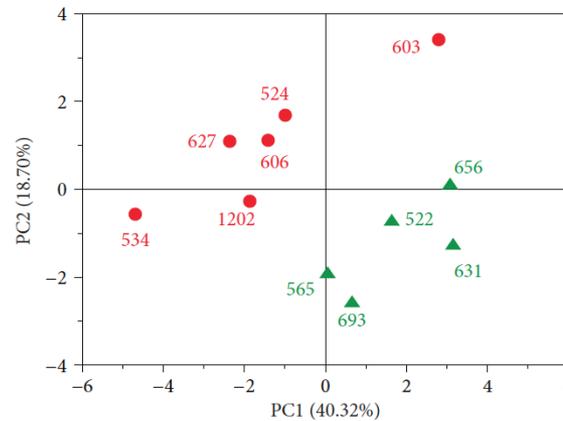


PCA Analysis – Media and Adventitia

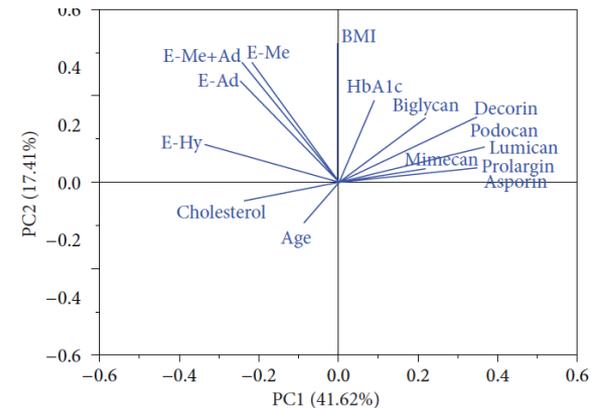
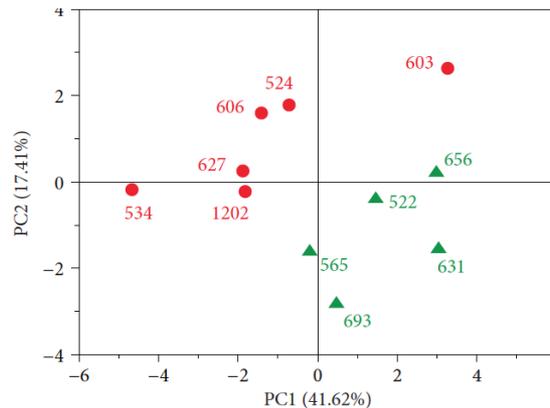
Score Plots

Loading Plots

PWV and Elastic modulus



Elastic modulus only



- Medial layer nanomechanics of the IMA also separate the group

Conclusions

- Nanomechanical data in the IMA correlates with carotid-femoral PWV.
- IMA reflects changes across the vasculature although it is not an elastic vessel and hence does not contribute to PWV measurements.
- Collagen fibril diameter and D-Period ('Collagen quality') served as a suitable method for detecting alterations in the local adventitial environment.

Acknowledgements

Dr Zhuo Chang (Former Dual PhD Student
University of Liverpool/NTHU, Taiwan)

Professor Lars Melholt Rasmussen

Maria Lyck Hansen

Hans Christian Beck

CIMA
Centre for Individualized Medicine
in Arterial Diseases



Dr Steve Barrett (Physics)

Dr Eva Caamaño-Gutiérrez (Institute of Integrative Biology)

Dr Ya Hua Chim (School of Engineering)