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Optical coherence elastography for cellular-scale stiffness imaging of mouse aorta

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INTRODUCTION

- Cellular-scale imaging of the mechanical properties of tissue has helped to reveal the biophysical origins of disease
- Cellular-scale resolution has yet to be achieved in intact tissue volumes
- We demonstrate optical coherence elastography toward volumetric imaging of stiffness at a 15-µm resolution in intact aorta from a mouse model of hypertension

OPTICAL COHERENCE MICROSCOPY

STRUCTURE

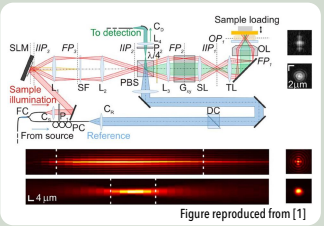


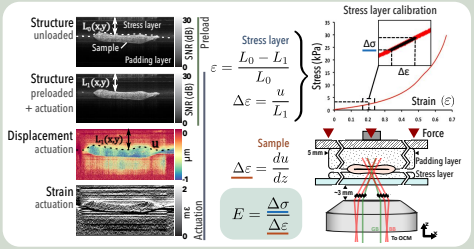
Figure reproduced from [1]

- Measures time-of-flight of light waves scattered from tissue microstructure.
- Three-dimensional
- Label-free
- Sub-2 µm resolution over 1x1x0.1 mm field of view

COMPRESSION ELASTOGRAPHY

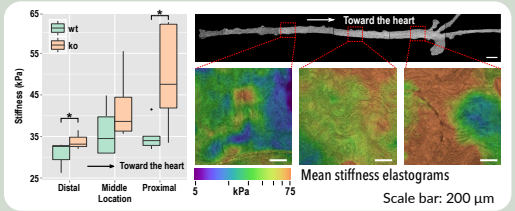
MECHANICS

- Elastography - mapping tissue mechanics into an image.
  1. Tissue is loaded and imaged.
  2. Local strain is calculated from the slope in tissue displacement.
  3. Stress is calculated by consulting stress layer's pre-characterised stress-strain curve.
  4. Stiffness (Young's Modulus) is calculated as stress / strain [2]



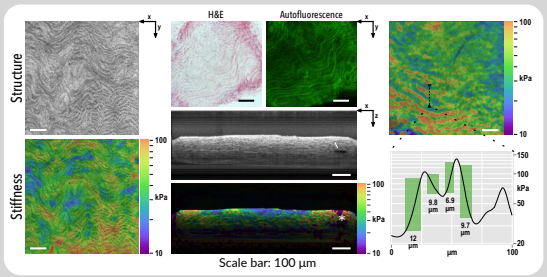
MOUSE MODEL

- Mouse model: Regulator of G protein signalling (RGS)5-knock out (ko); vs. wild type (wt).
  RGS5 linked to vascular stiffness, contractility and remodelling. [3]
  RGS5 deficiency → hypertension, medial hypertrophy, fibrosis.

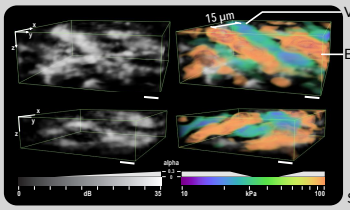


Aorta in RGS5-ko mice is stiffer to wt, particularly near the aortic arch; in RGS5-ko mice, aorta stiffens with proximity to the heart.

RESULTS



Wavy appearance is likely to be the elastin as part of the elastin lamellae, interleaved with vascular smooth muscle cells



Vascular smooth muscle cells

Elastin lamellae

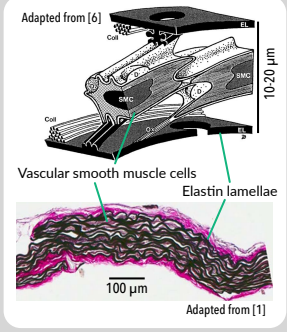
- Sub-15 µm resolution
- 10-20 µm corresponds to spacing between elastic lamellae
- < 7 min acquisition

Scale bar: 10 µm

OCE identifies micro-mechanical features

- 8 local fibrous reagions (6 in ko)
  Stiffer: 70-150 kPa
- Regions of lipid formation in ko and wt
  SEM images of ultrastructure have [4] revealed lipid deposits; growing in size in early fibro-lipid development

OCE may be useful in studying plaque formation



DISCUSSION

- RGS5 is under epigenetic control
- [5] Regional differences may manifest as phenotypic differences in vSMC
  Ratio of elastin to smooth muscle decreases away from the heart
  Stiffness increases away from the heart with age; young aorta is more homogenous

RGS5 likely has a role in normalising stiffness

- We have developed a system for 3D mapping of tissue structure (sub-2 µm resolution) and stiffness (15 µm resolution) over 1x1x0.1 mm field of view.
- It has potential in elucidating the role and the control of stiffness in cardiovascular function, and aid the development of targeted treatment strategies

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