A VEIN ATTEMPT?

DEVELOPING A MACROFLUIDIC MODEL OF ARTERIOVENOUS FISTULAS TO STUDY FLOW-MEDIATED ENDOTHELIAL CELL SIGNALLING

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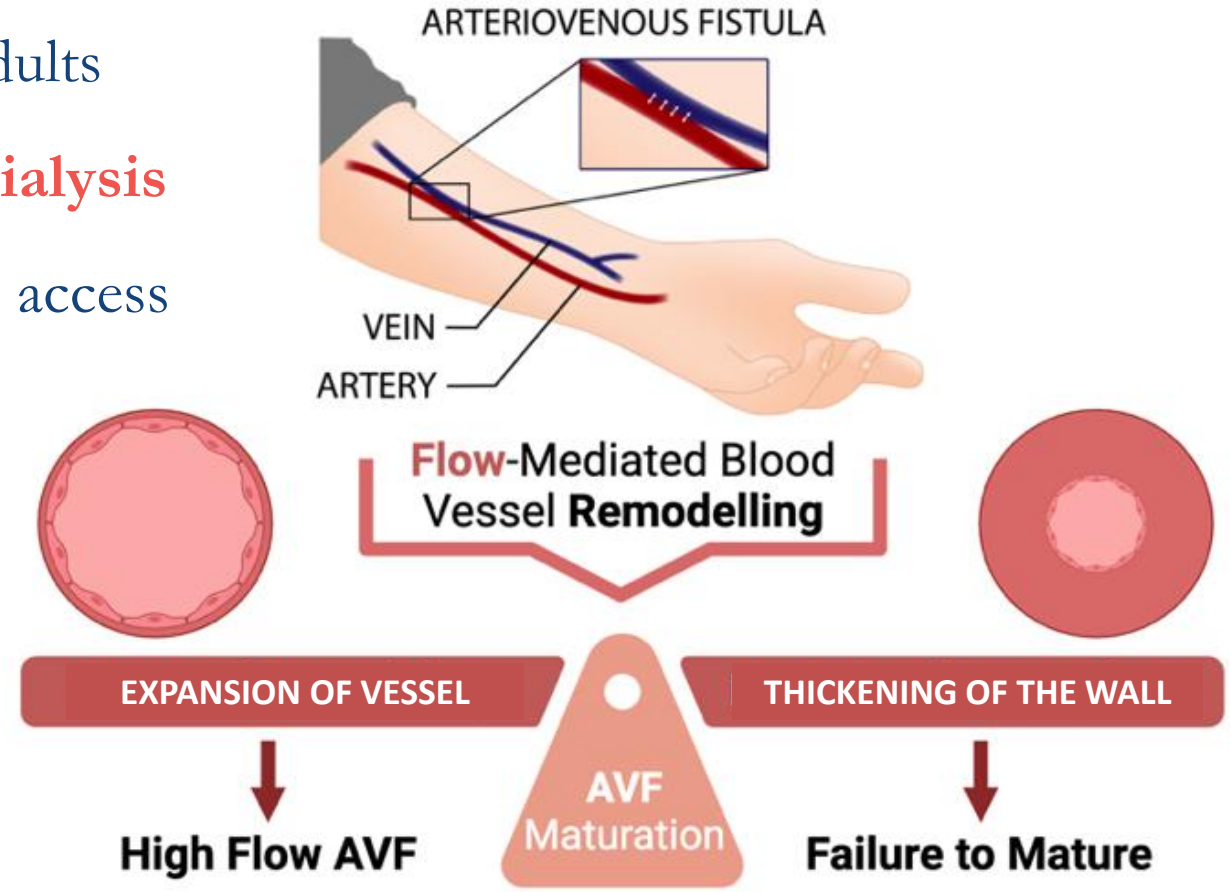
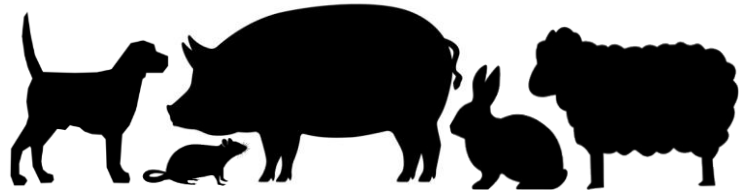
WHY THIS MATTERS

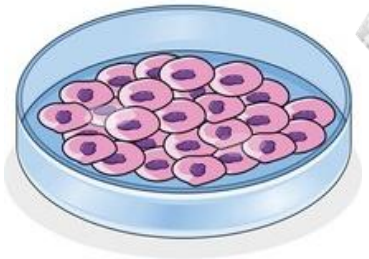
- Chronic kidney disease affects >10% of adults
- Most end stage kidney disease → **haemodialysis**
- Haemodialysis needs **reliable** bloodstream access
- **Arteriovenous fistulas (AVF)** preferred
- Up to 60% of AVFs will **NOT WORK**
  - Vascular access catheters
    - ↑ infections + ↑ death
  - More surgeries
  - High cost to healthcare system

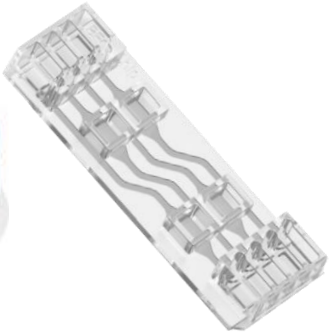


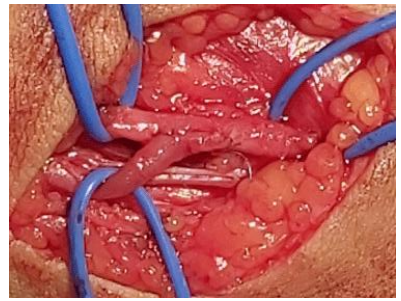
NO IDEAL MODELS EXIST

- Computational fluid dyanamics = **no biology**
- Animal models = **?ethics/practicalities**
- 2D culture = **limited interpretability**
- Microfluidic devices = **not true geometry**
- Biopsy of new AVFs = **unsafe, ?ethical**









- A **patient-specific <u>MACROFLUIDIC</u>** device:
  - **QUICK and UNLIMITED** experiments
  - Effect of **geometry**
  - Effect of **flow**
  - Effect of **biochemistry** (uraemia)

UNSW SYDNEY

WHERE ARE WE UP TO?

1

WE CAN CAPTURE AND FABRICATE PATIENT-SPECIFIC MODELS

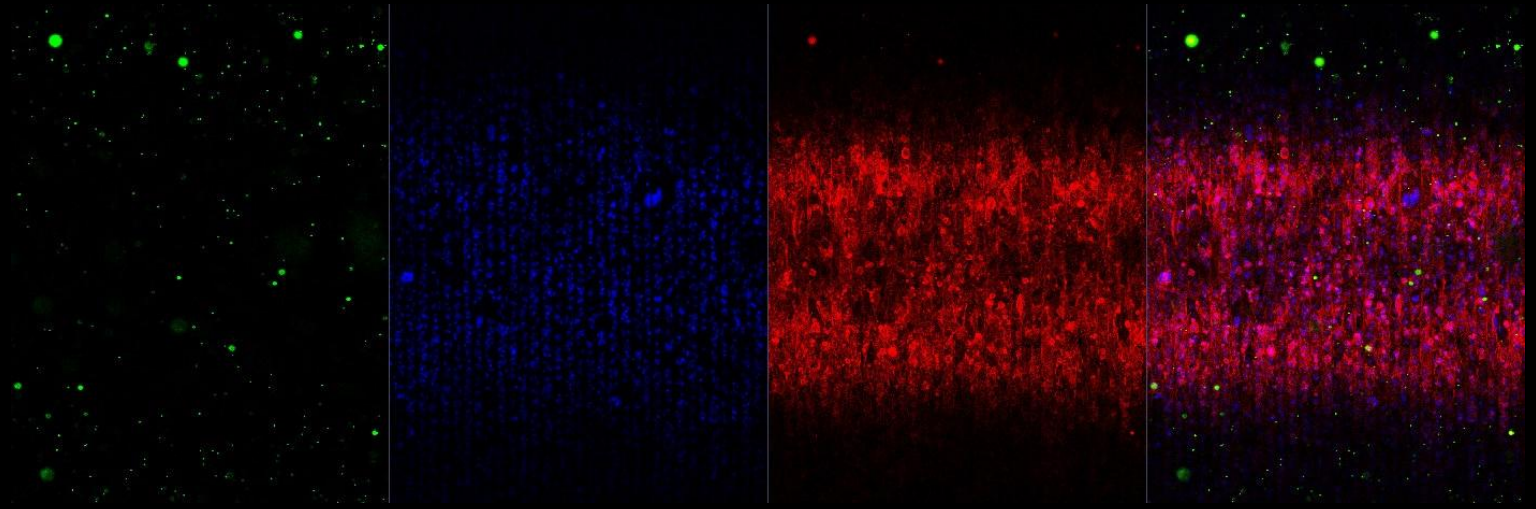
2

THE CELLS ARE ALIVE AND RESPOND AS EXPECTED

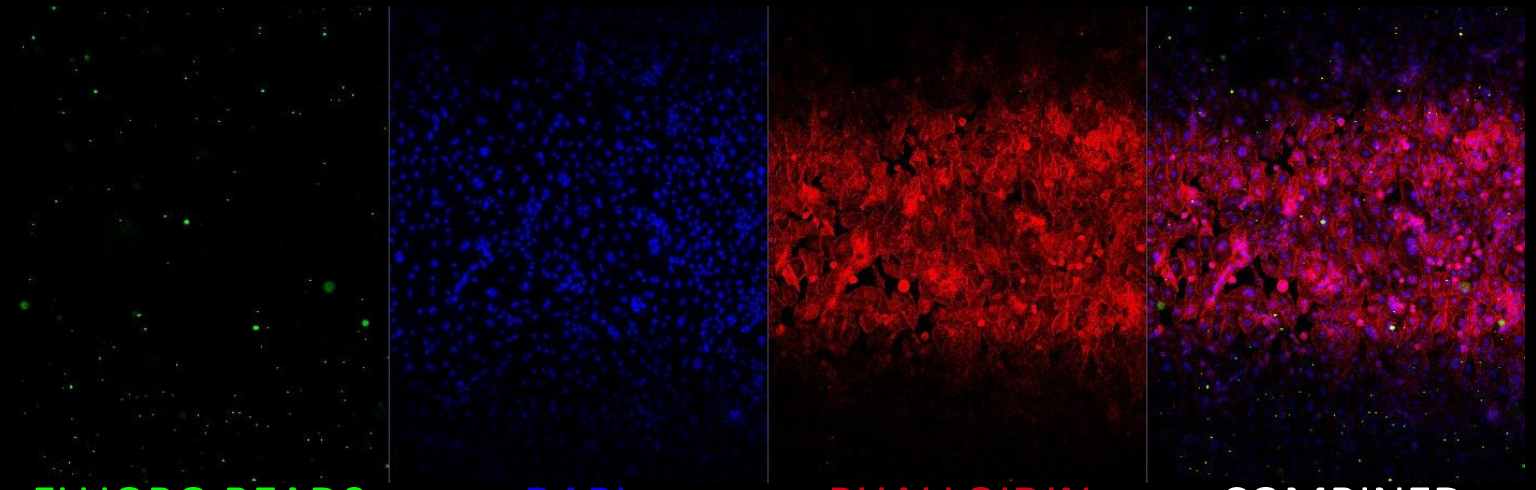
3

WE CAN CONTROL THE FLOW: CONTINUOUS AND PATIENT-SIMILAR

SIMPLIFIED VESSEL - STATIC CONDITIONS



SIMPLIFIED VESSEL – 100 mL/min FLOW – 24H

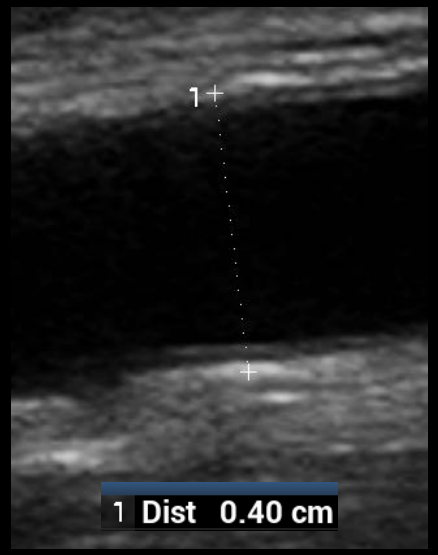


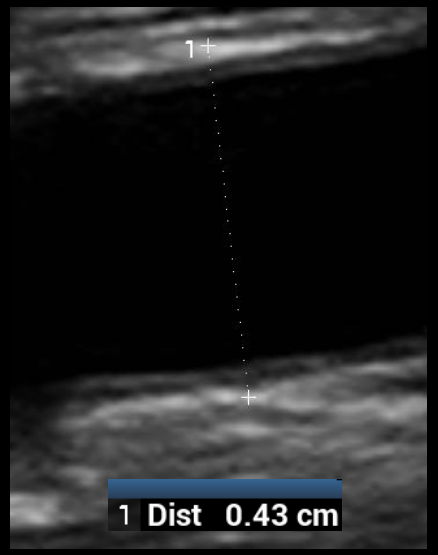
FLUORO BEADS DAPI PHALLOIDIN COMBINED

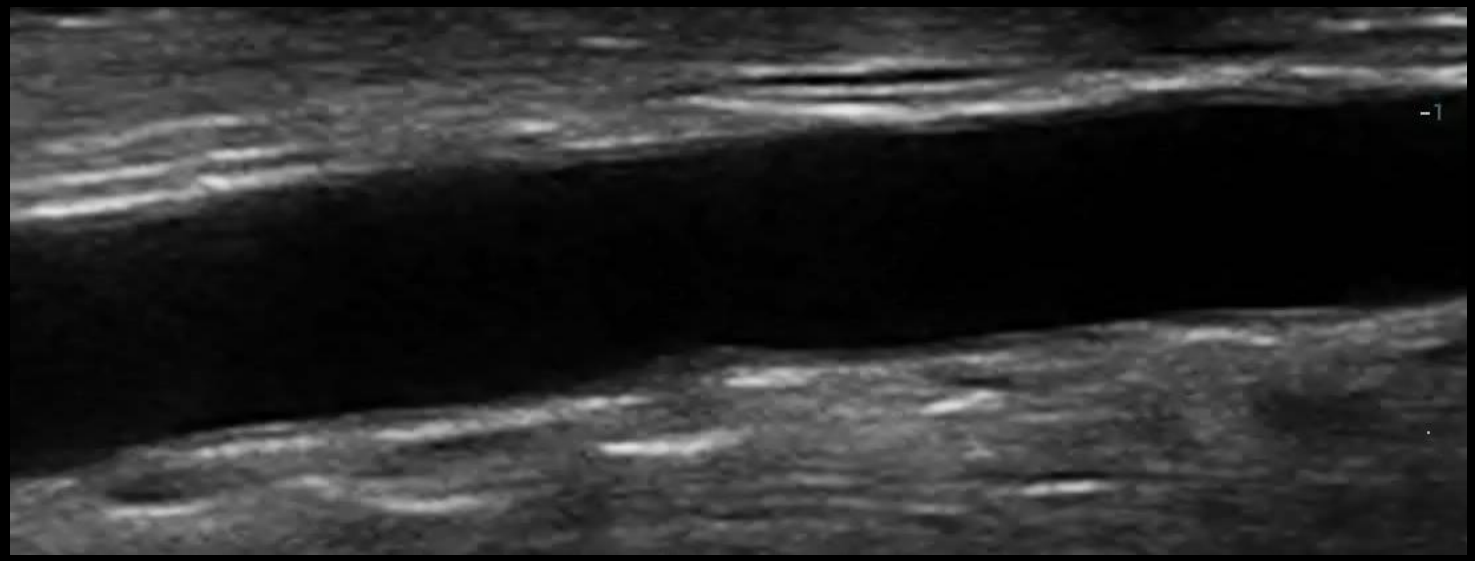
WHAT DO WE NEED?

- [ ] What about the blood vessel walls?
- [ ] What happens to the cells?

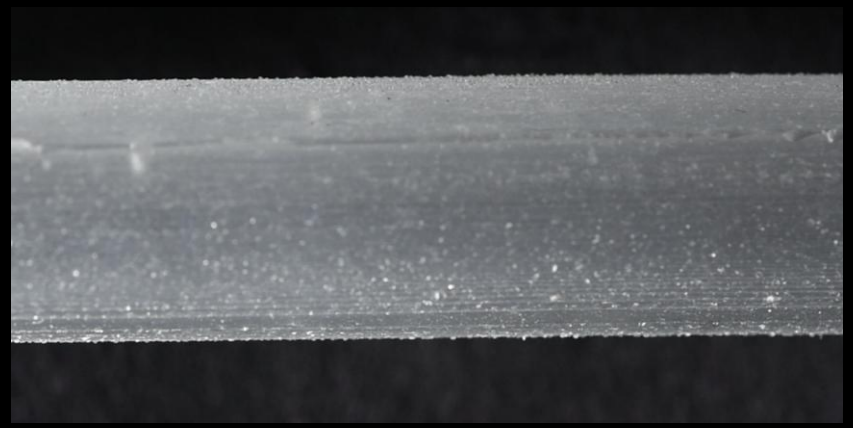
PATIENT BLOOD VESSEL



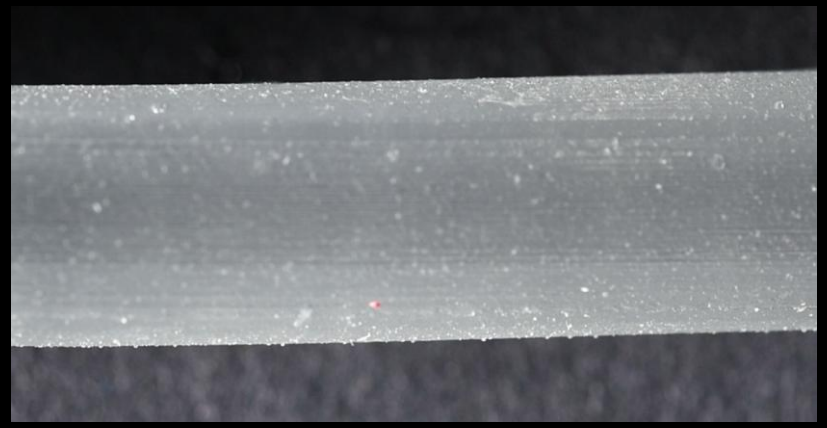




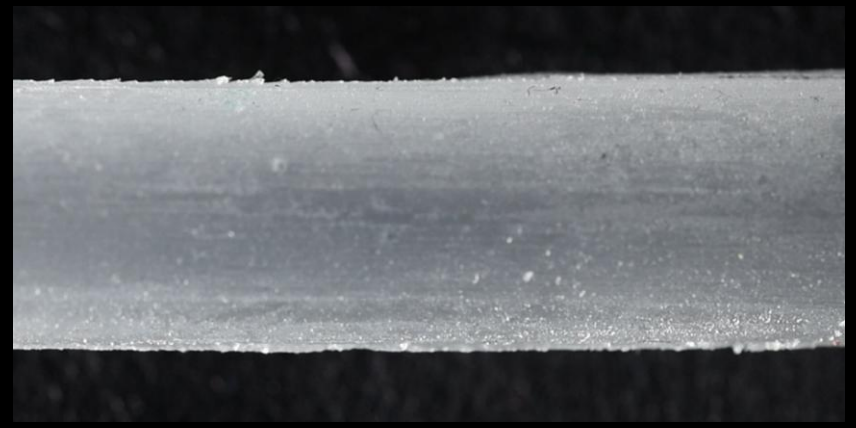
SILICONE IN VITRO MODEL + PULSATILE FLOW



5:1 Silicone MIX



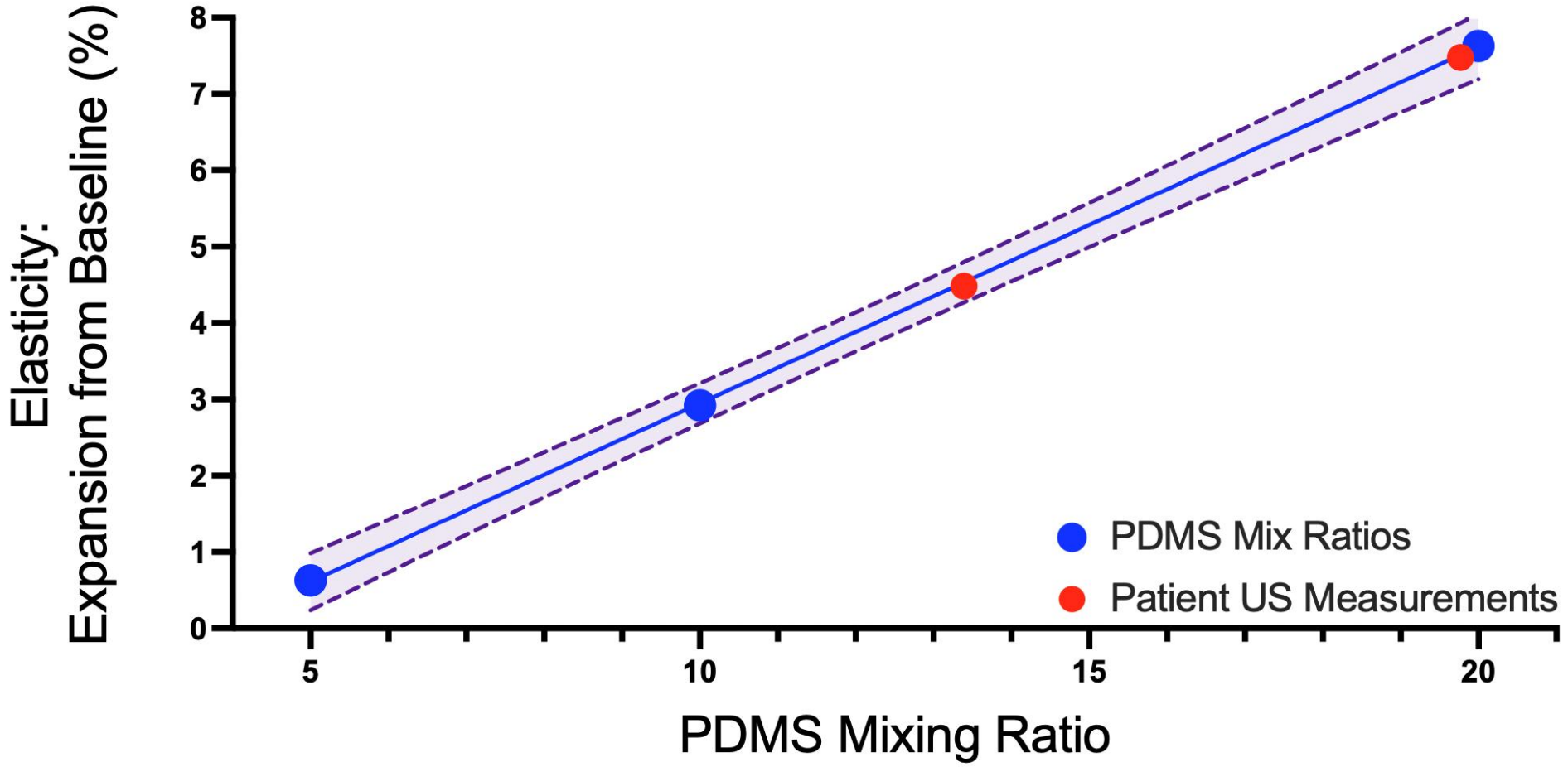
10:1 Silicone MIX

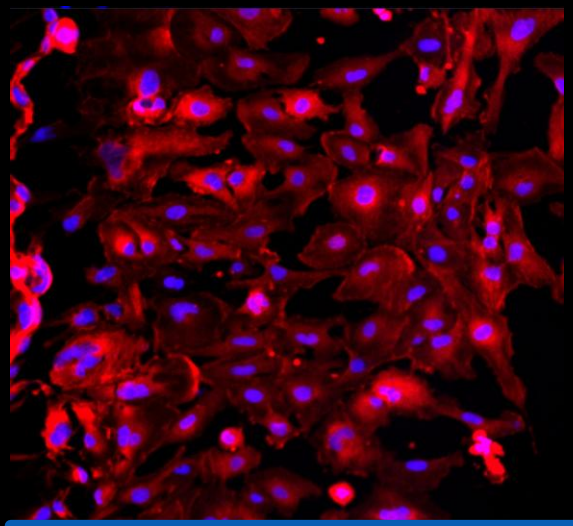


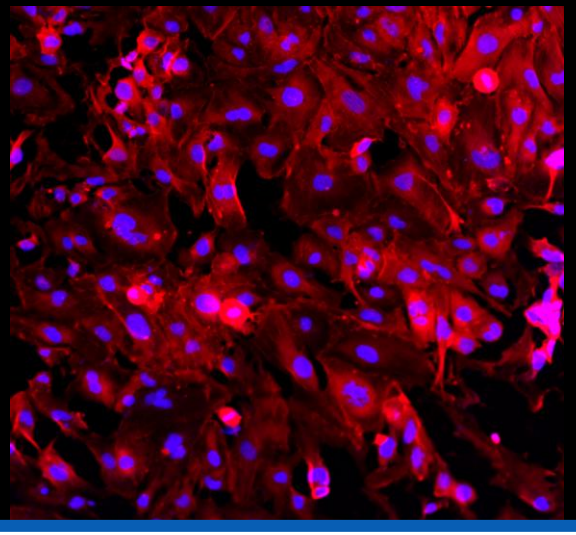
20:1 Silicone MIX

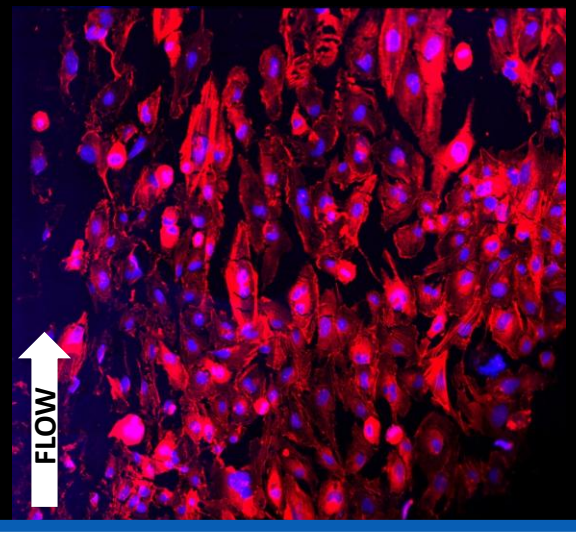
UNSW SYDNEY

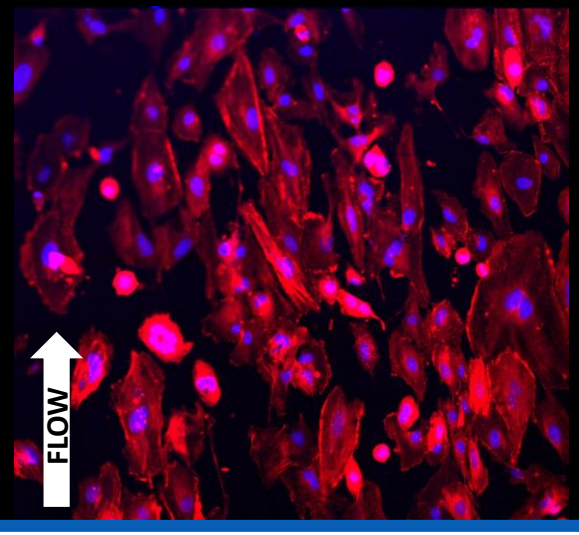
DICTATING ELASTICITY!



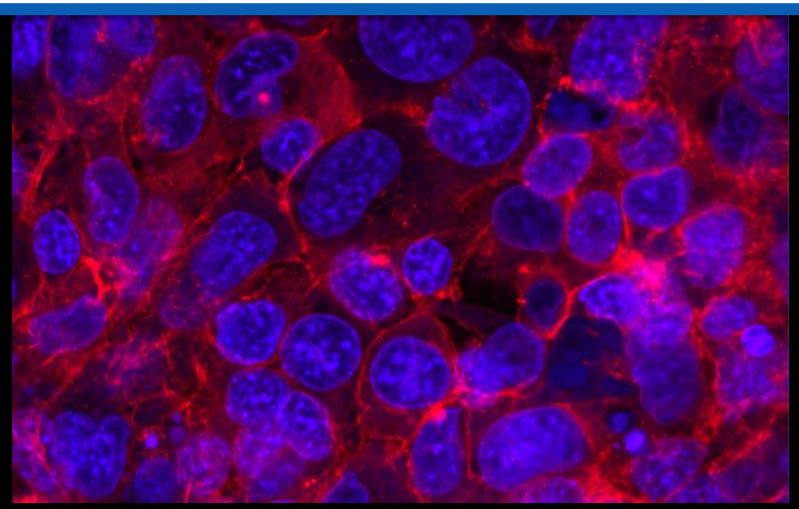


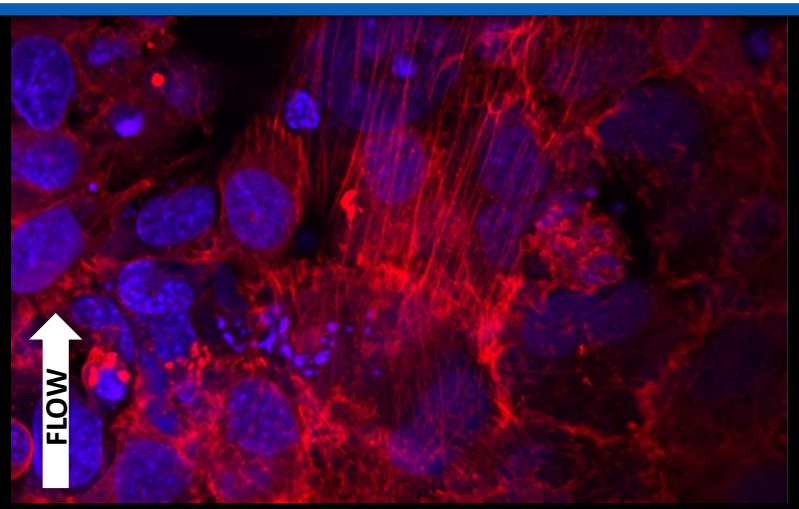




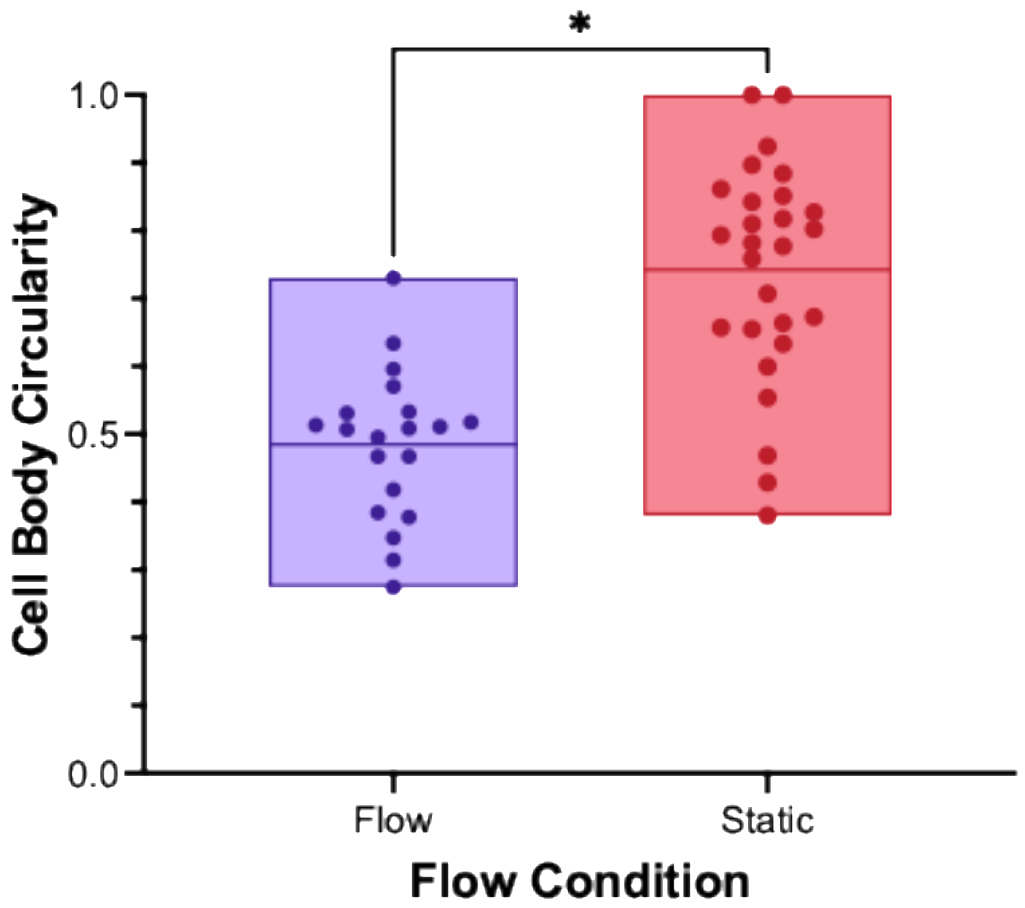


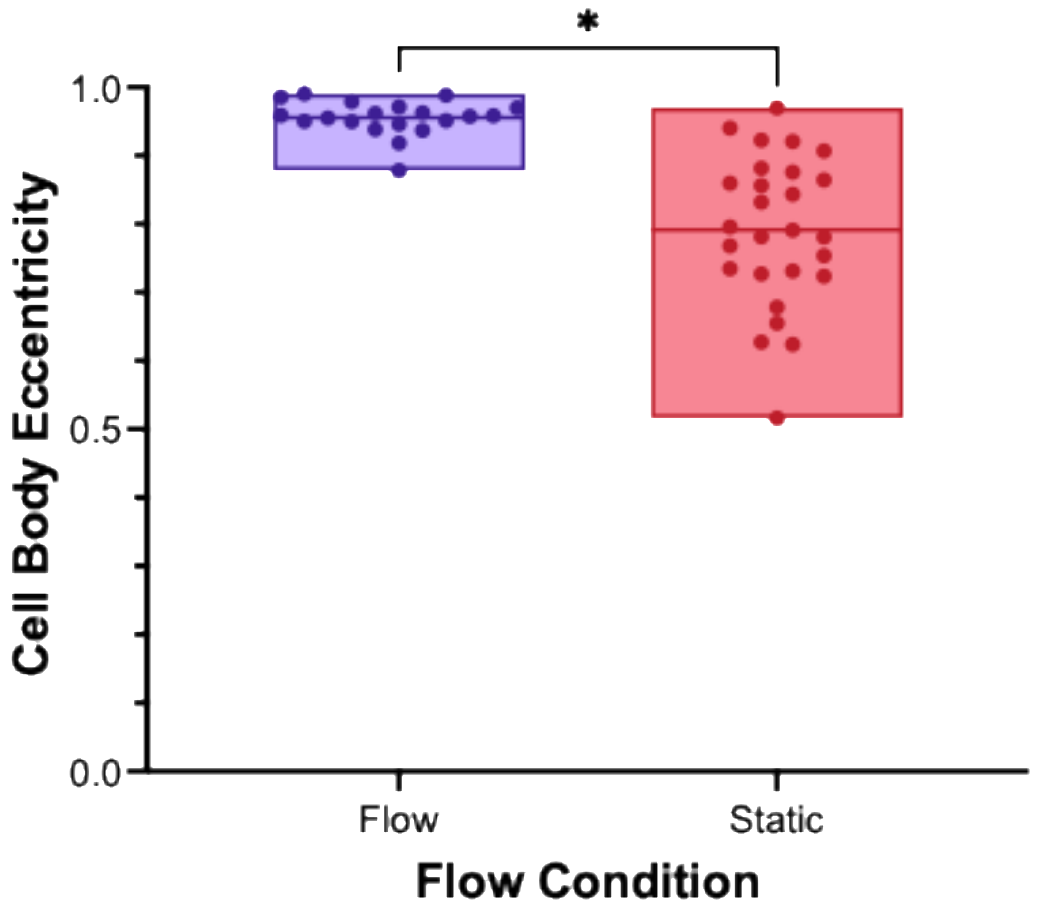
THE CELLS CHANGE IN FLOW
(as expected)





FLOW = ↓ CIRCULAR, ↑ ELONGATED



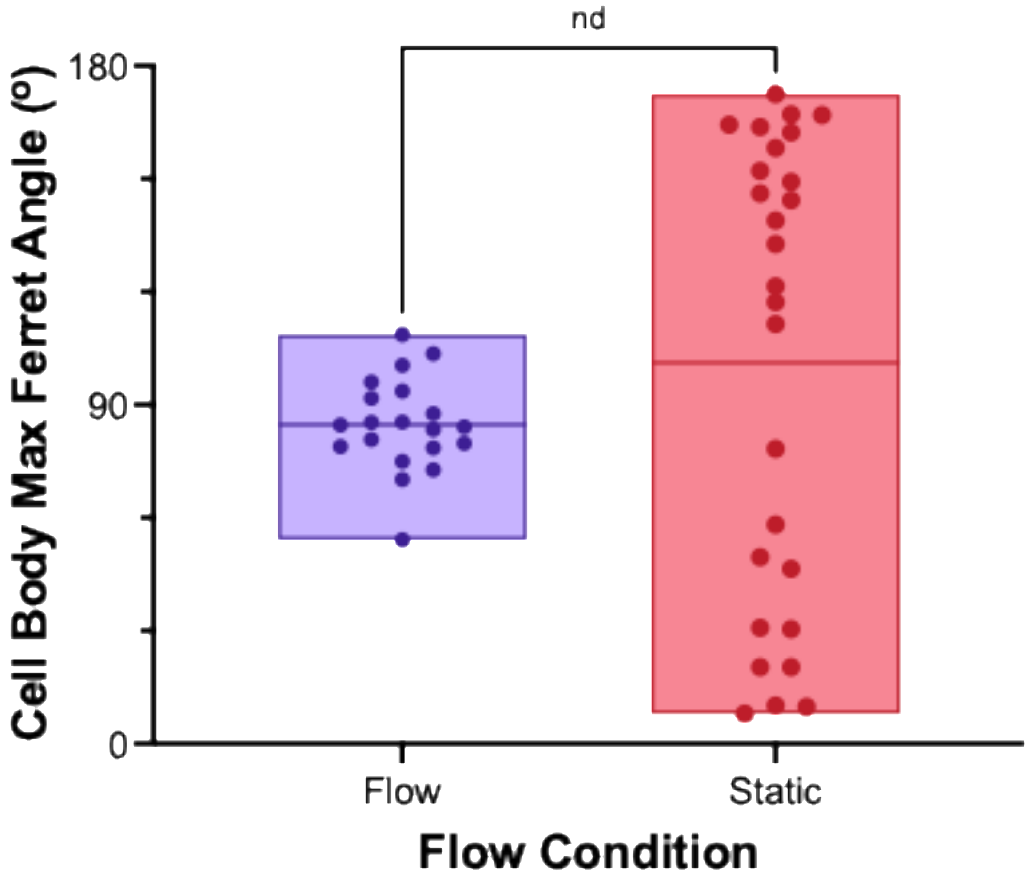


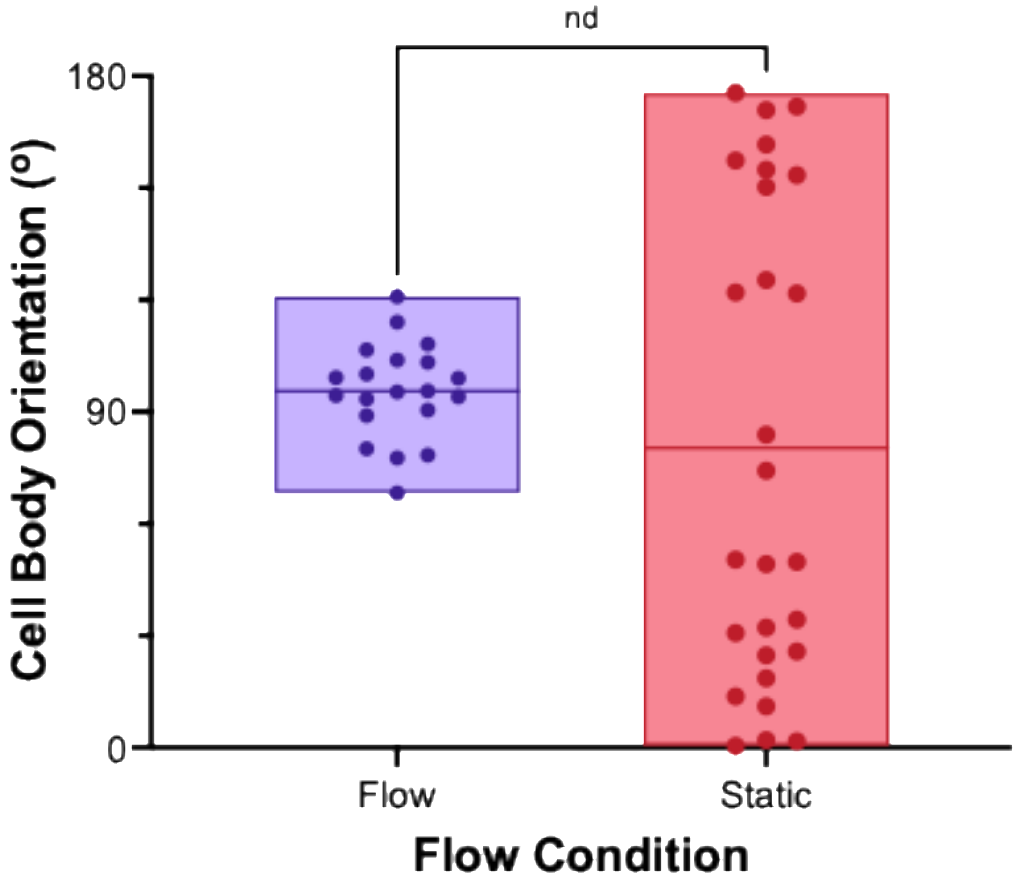
LESS CIRCULAR

MORE ELONGATED

*, p<0.001 by two-tailed Mann-Whitney U Test

CELLS LINE UP IN FLOW



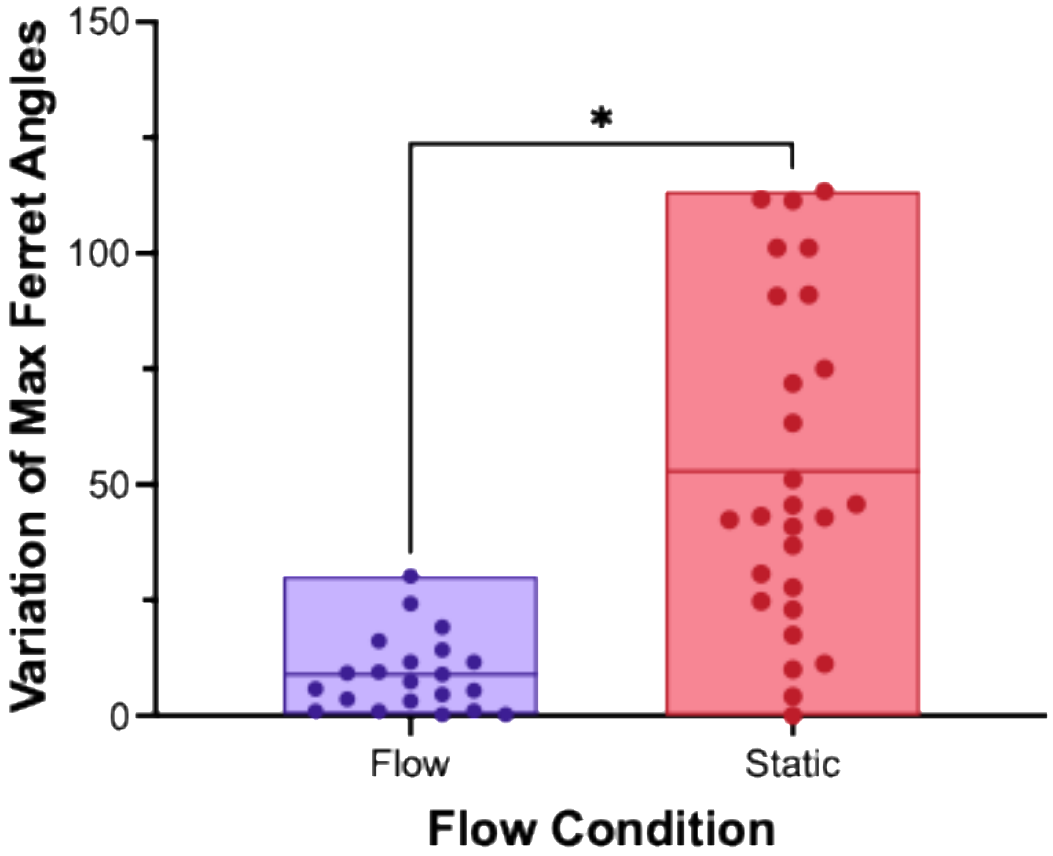


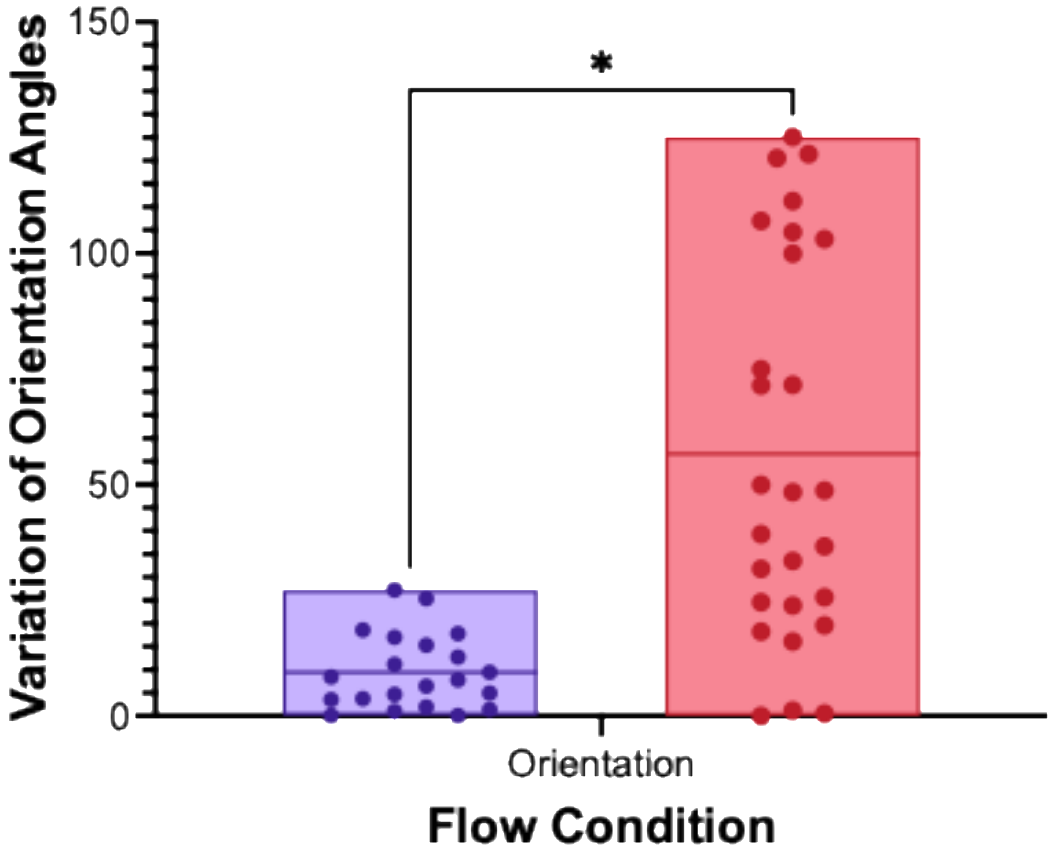
∠ from horizontal → cell long-axis:
consistent in **FLOW**, variable in **static**

nd, p>0.05 by two-tailed Mann-Whitney U Test

UNSW SYDNEY

CELLS LINE UP IN FLOW



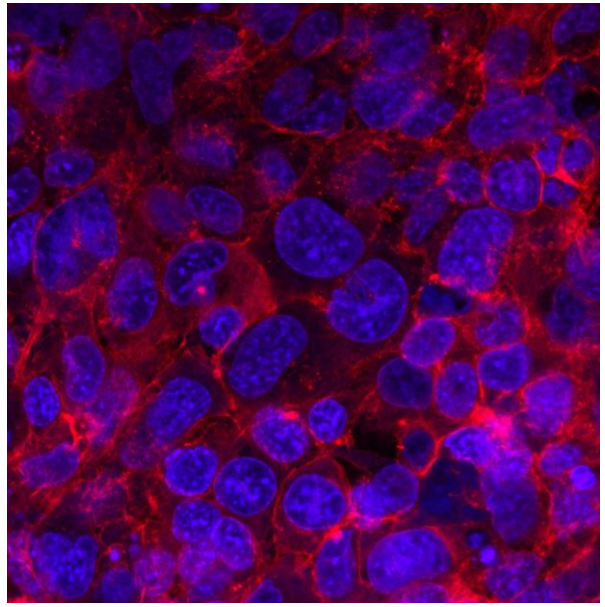


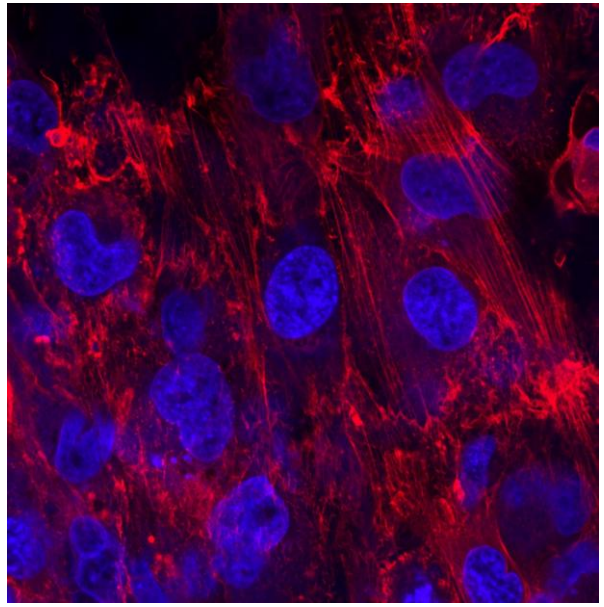
*Brown–Forsythe test used to assess differences in variance

Orientation Parameters: Deviation from median ↓ in FLOW

SO… WHAT'S NEXT

- MACROfluidic in vitro model
  - Scan, segment, and print
  - Cast in elastomer
  - Modify the elastomer surface
  - Grow endothelial cells + subject to flow
  - Can replicate physiologic flow
  - Can model blood vessel elasticity
- Future direction = MORE biology…
  - Characterise cells further *(RNAseq)*
  - ?magnitude of flow +/- uremia
  - Spatial changes in AVF geometry
  - Co-culture (VSMC)? Dual layer?

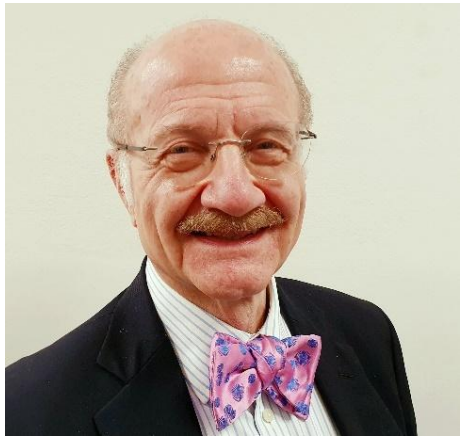




THANK YOU
for your attention

NEPHROLOGY

Dr. Jonathan Erlich



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Dr. Blake Cochran

ENGINEERING

Prof. Tracie Barber

RACP Specialists. Together
Jacquot Research Entry Scholarship

BAXTER CHARITABLE FOUNDATION
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