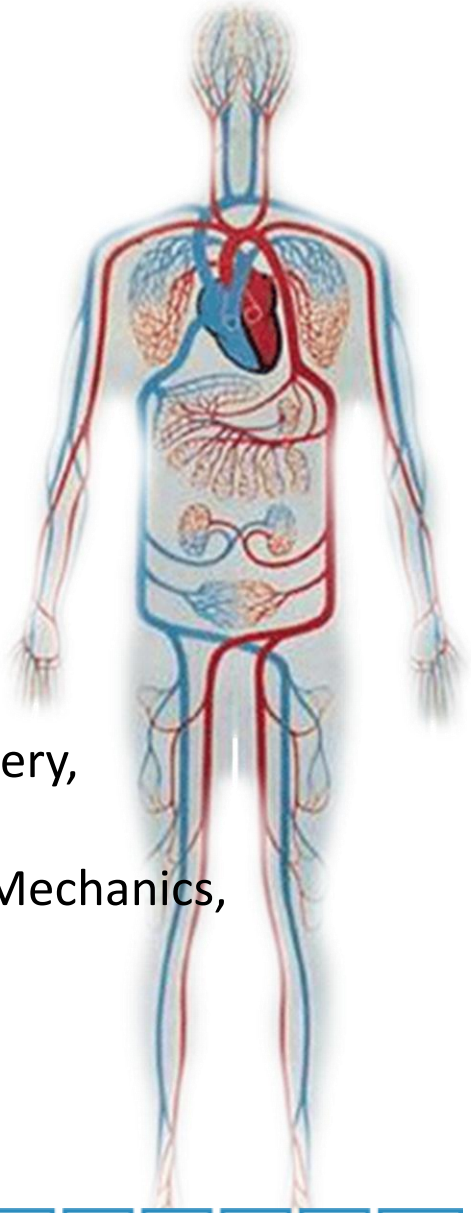
# Multiscale Computational Modelling in Biomechanics of Cardiovascular Diseases and Therapies

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www.biomechanics.uct.ac.za

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Centre for Research in Computational and Applied Mechanics

# Group & Acknowledgements

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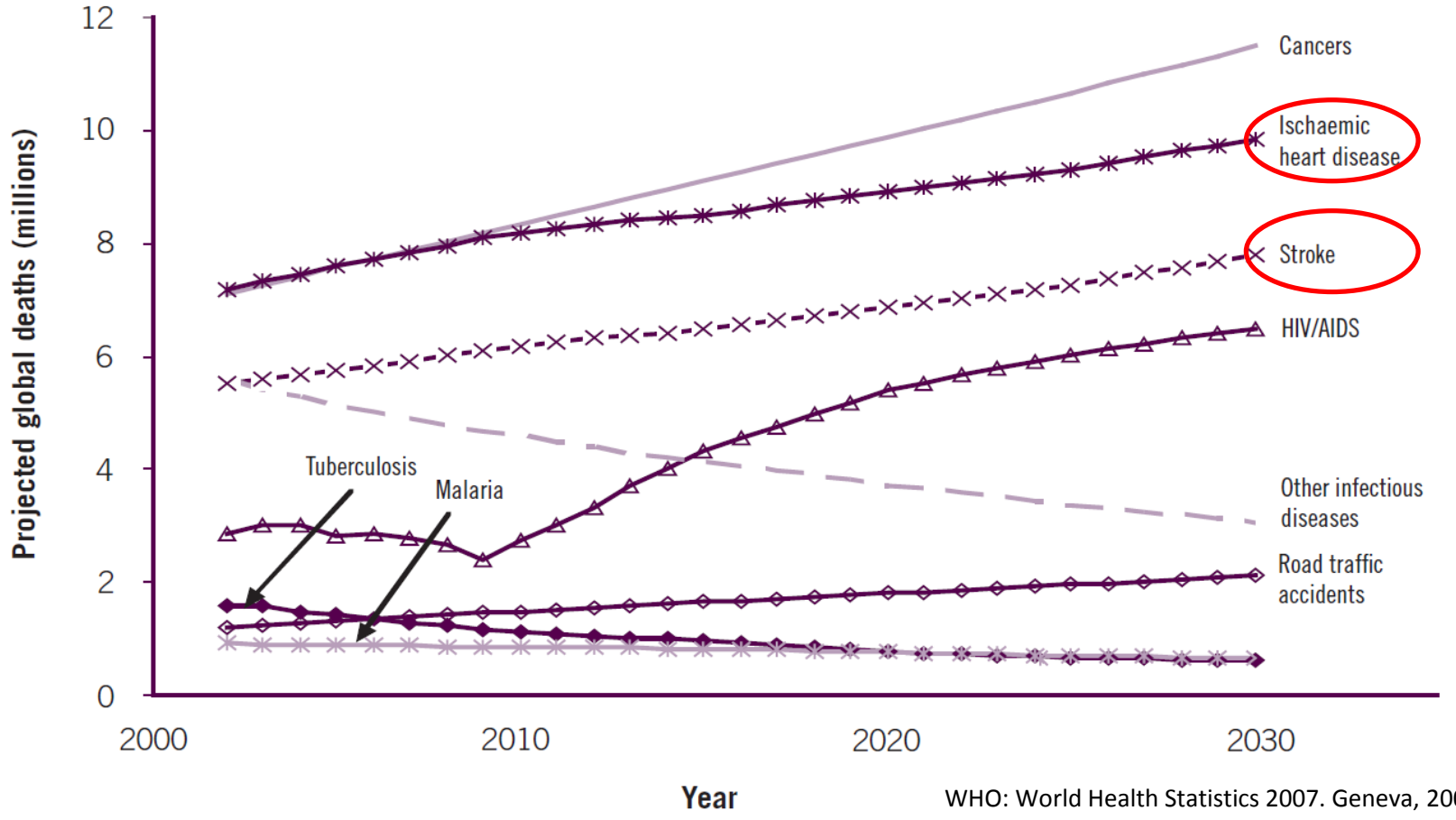
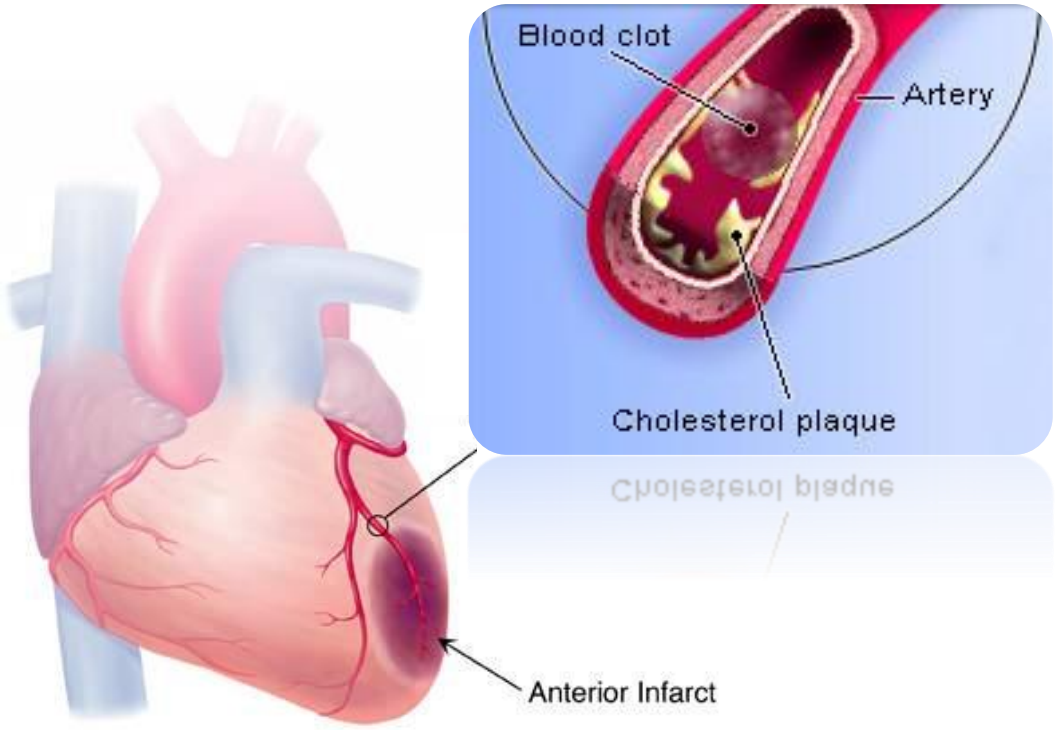
- University of Cape Town
- Medtronic Inc

# Projected global deaths for selected causes of death, 2002–2030




WHO: World Health Statistics 2007. Geneva, 2007

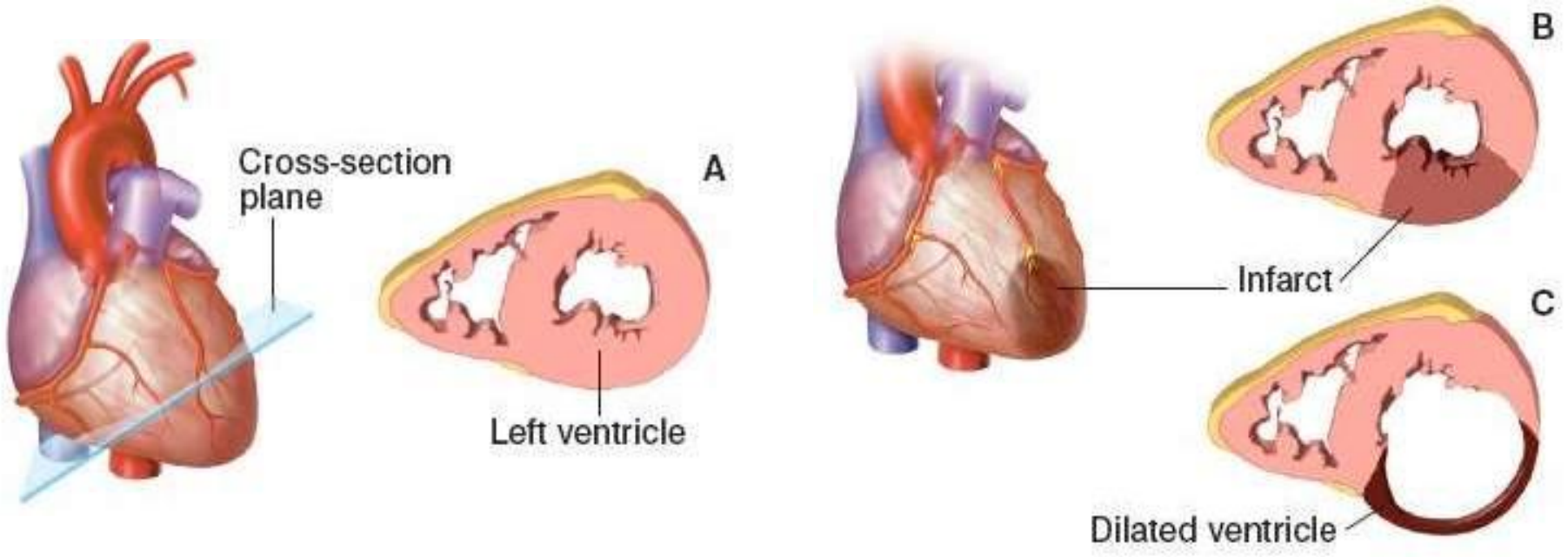
# Myocardial Infarction = Heart Attack



# Post-infarct Remodelling of the Heart

Healthy

Infarcted

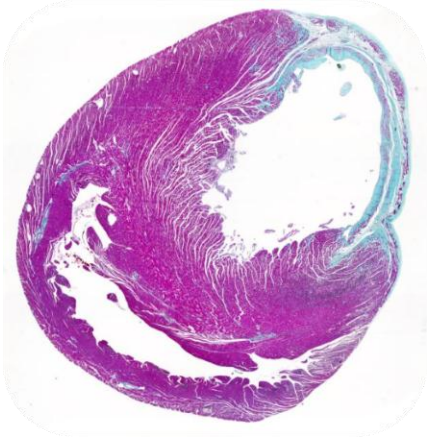


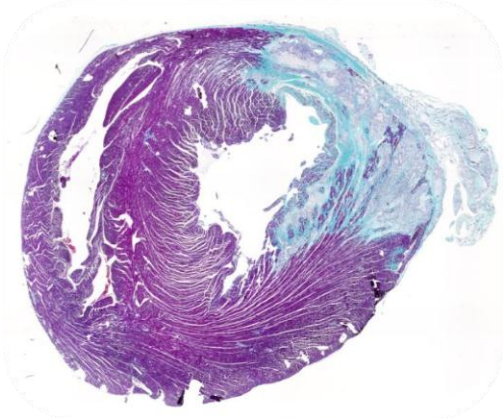
# Therapies for MI

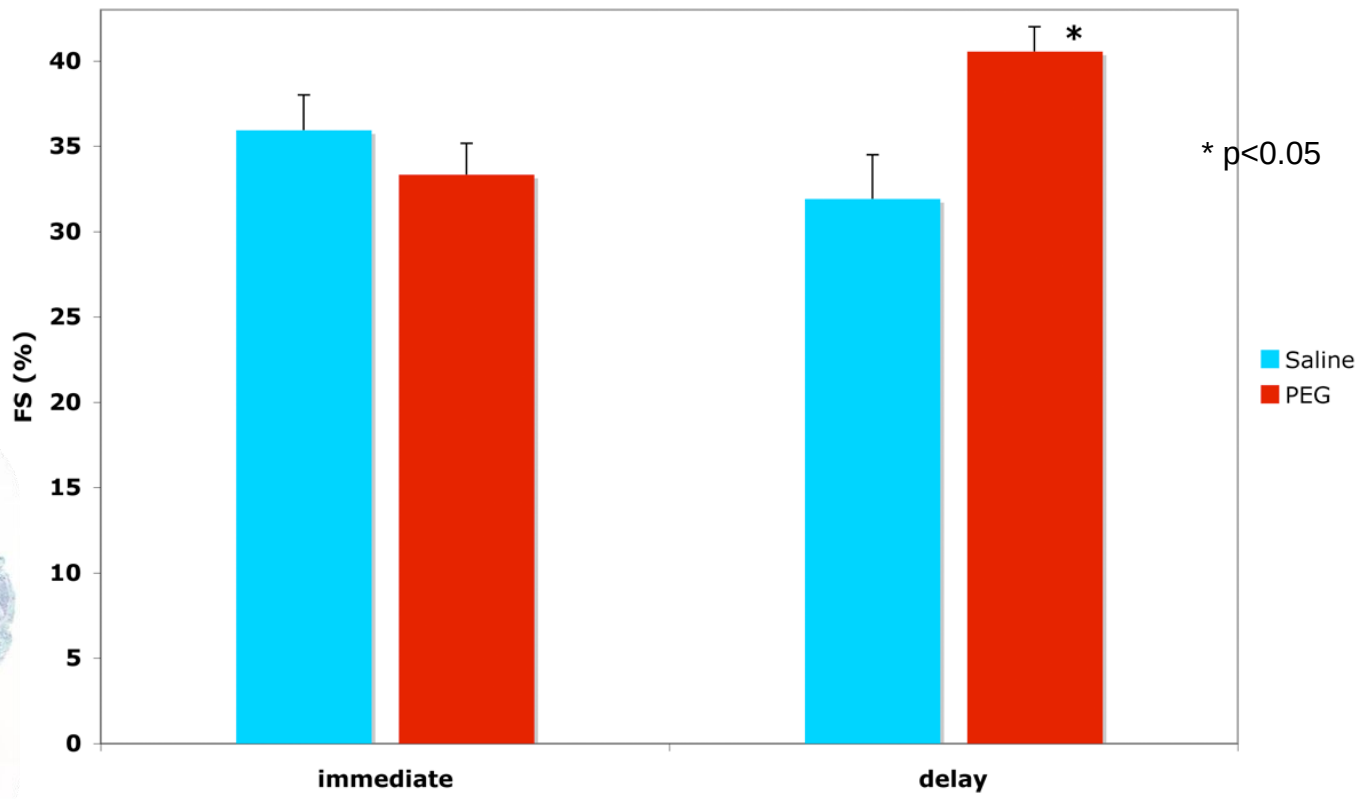
- Aim: Prevention of adverse remodelling of the heart
- Cell delivery therapy
  - Injection of cells with carrier medium into infarcted region of the heart
  - Positive outcomes
  - Mechanisms unclear

# Biodegradable Gel: Scar and Function

4 weeks after infarction





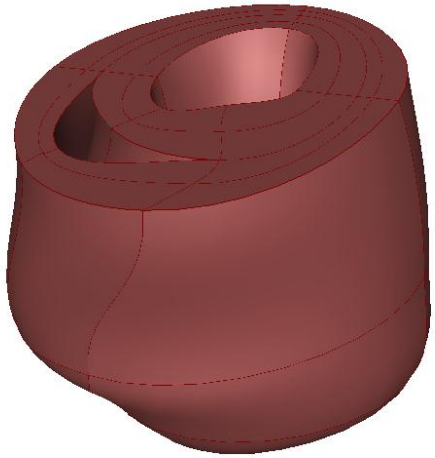


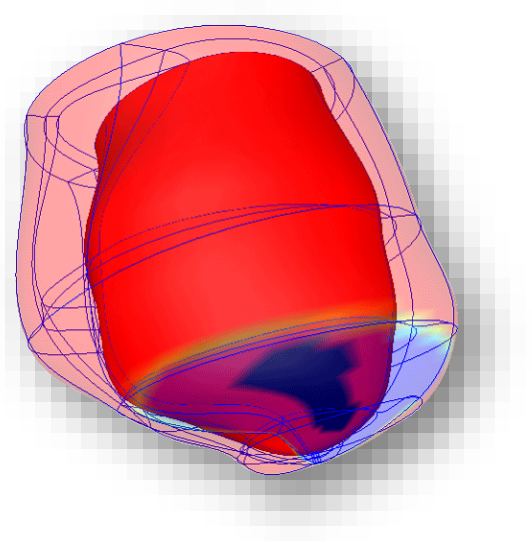

n=7-9

Kadner et al, Biomaterials, 2012

# Questions on Injection Therapy

- Contribution to mechanical and biological properties of the heart
- Properties of injectable biomaterials
- Timing of delivery
- Injection site
- Injection volume



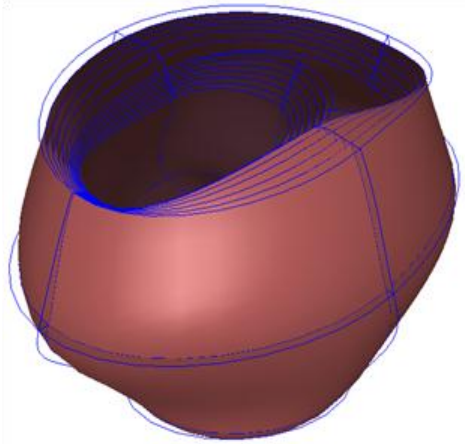


# Computational Mechanics of MI

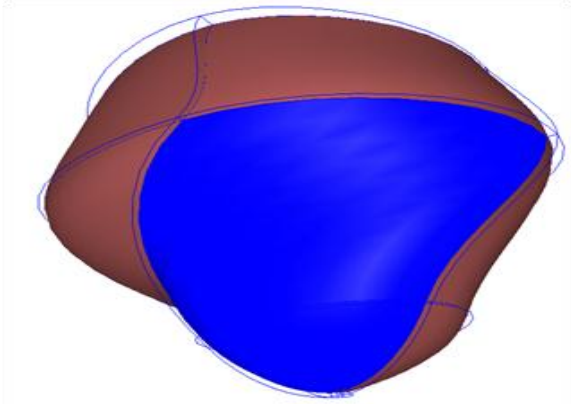
# Canine Biventricular Cardiac Model

- Myofibre representation
- Constitutive models
  - Passive strain energy function
  - Active contraction model
- Coupling to Windkessel circulation model

(Nielsen et al. 1991)



- Antero-apical infarct: 22% LV wall
- Infarct wall thinning
- Post-infarct LV dilation  100%

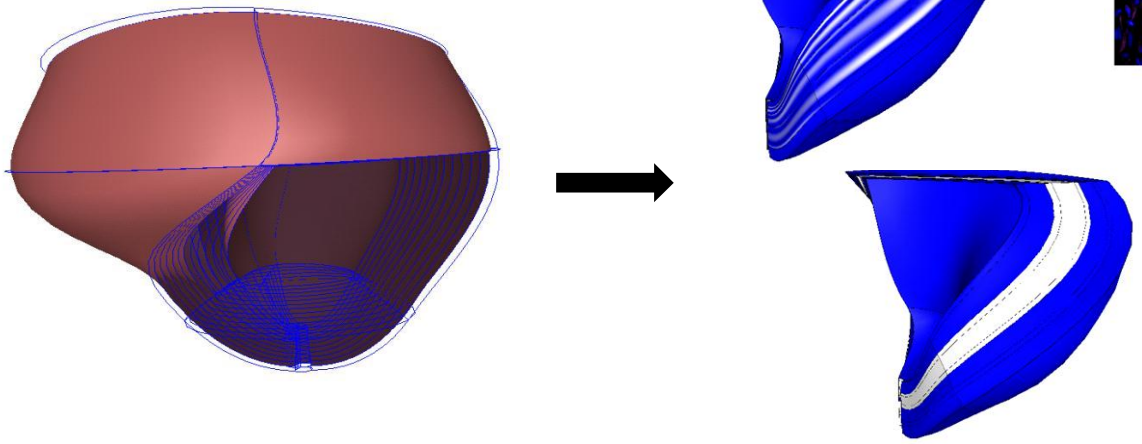


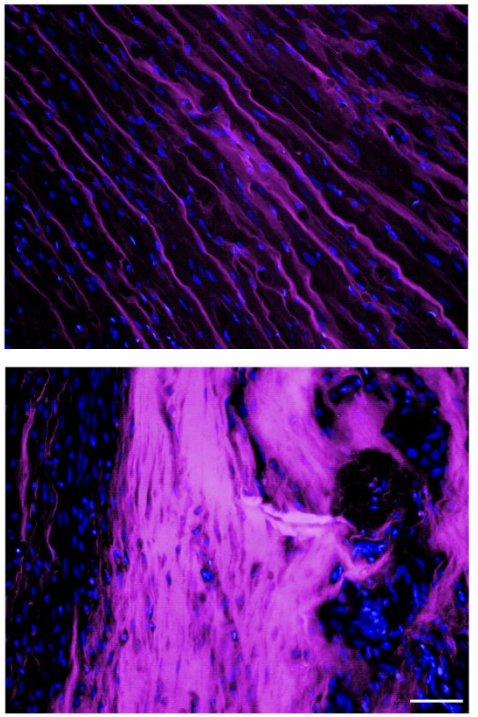
(Kortsmit, Davies, Miller, Franz)

# Hydrogel Injectates

**Gel inclusion in infarct region**

- Volume: 9.4 ml (7.1% of LV wall)
- Transmural distribution
  - 8 thin layers
  - Single bulk layer





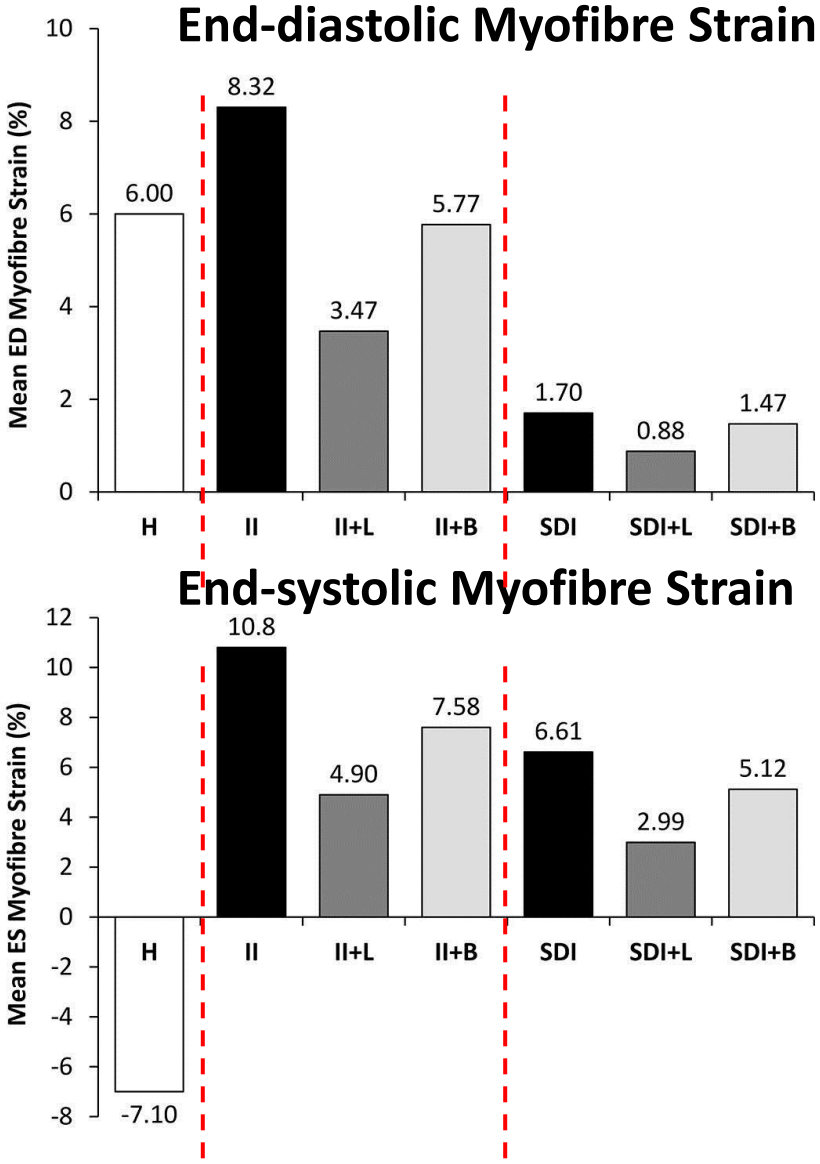
Kadner et al, Biomaterials, 2012

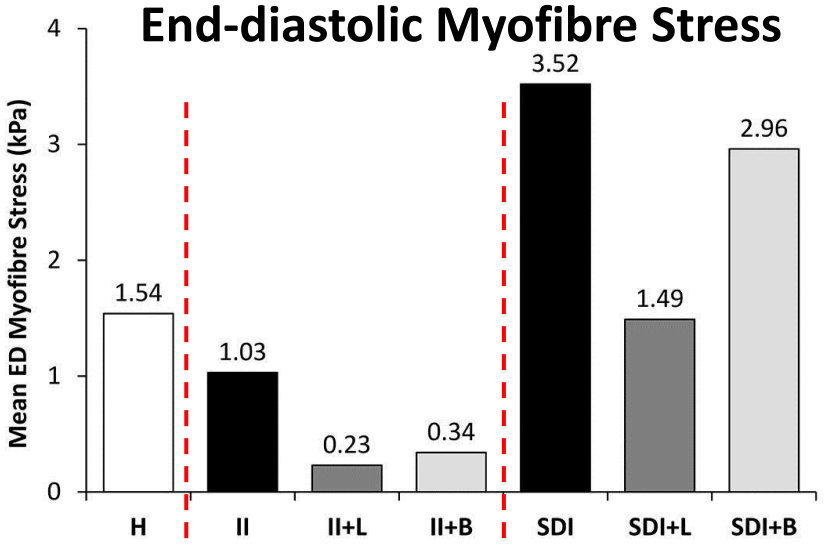
# Study Design and Ventricular Function

Time after coronary occlusion

| Case | | C | Functional Parameters | | |
|---|---|---|---|---|---|
| | | | $V_0$ (ml) | SV (ml) | EF (%) |
| **Healthy Control** | H | 0.88 | 13.9 | 15.2 | **35.6** |
| **Ischemic Infarct** | II | 0.88 | 17.8 | 6.61 | **15.5** |
| + layered gel | II + L | 0.88 | 16.7 | 7.02 | **17.7** |
| + bulk gel | II + B | 0.88 | 19.9 | 4.78 | **12.4** |
| **Scarred Dilated Infarct** | SDI | 8.80 | 39.4 | 9.28 | **11.8** |
| + layered gel | SDI + L | 8.80 | 27.9 | 13.0 | **19.0** |
| + bulk gel | SDI + B | 8.80 | 27.2 | 13.2 | **19.2** |

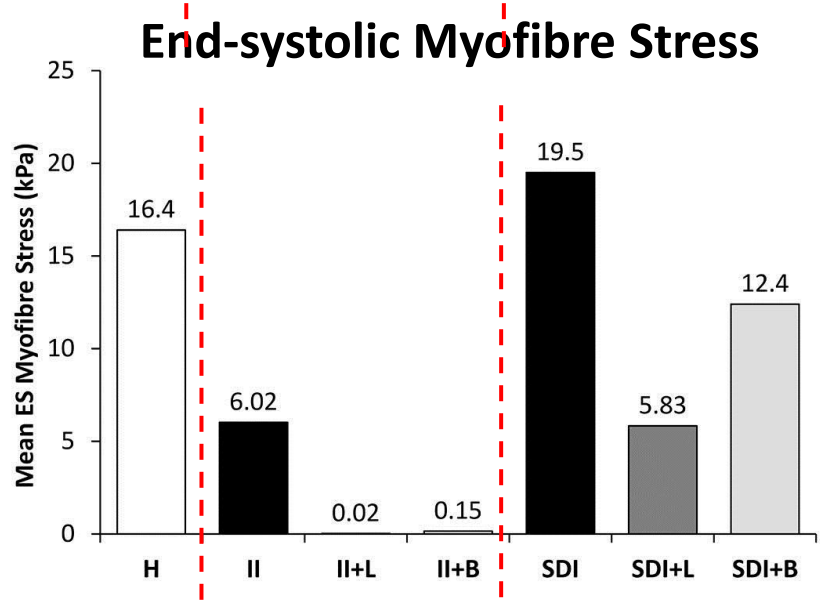
# Stress and Strain in Infarct Region

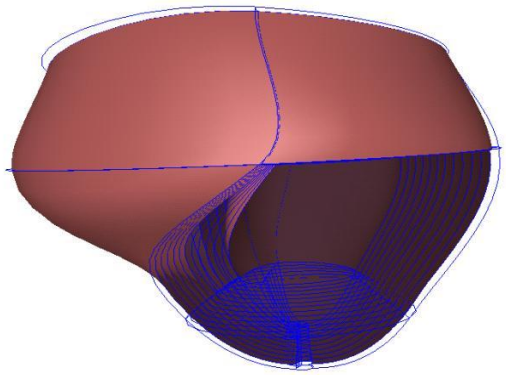


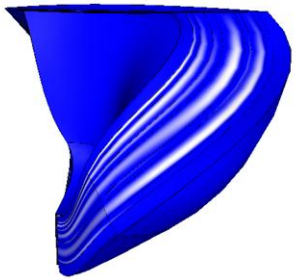



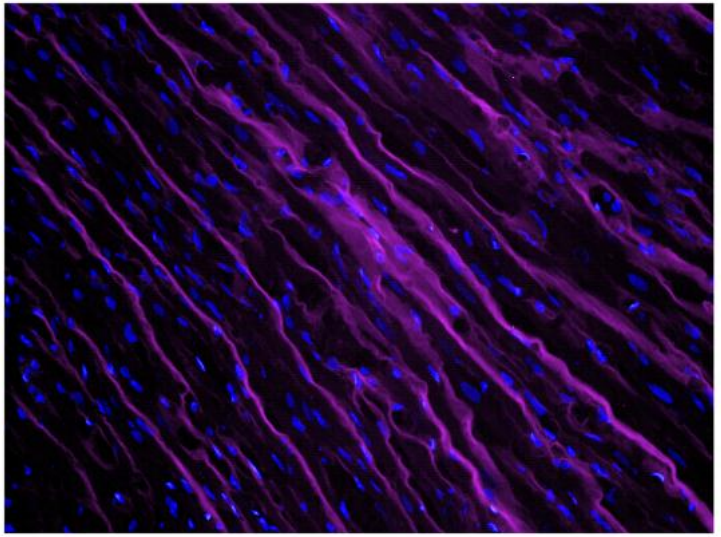






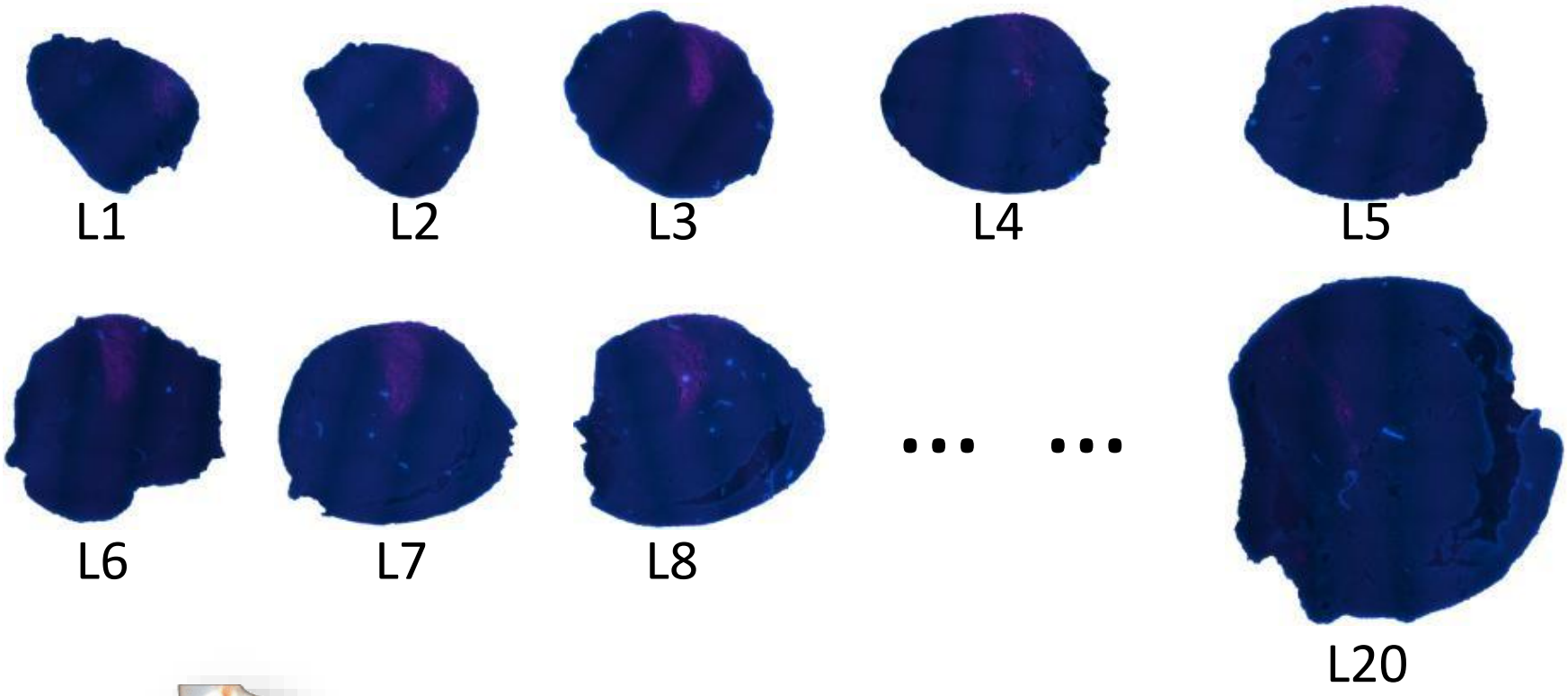


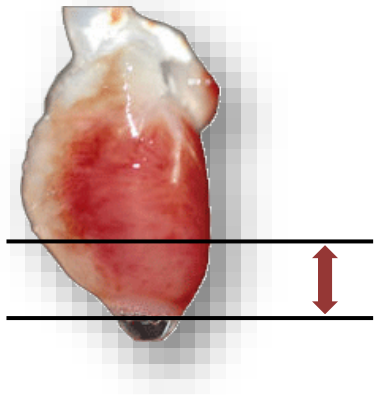




# MICRO-STRUCTURAL MODELLING OF BIOMATERIAL INJECTATE

# Injectate Reconstruction

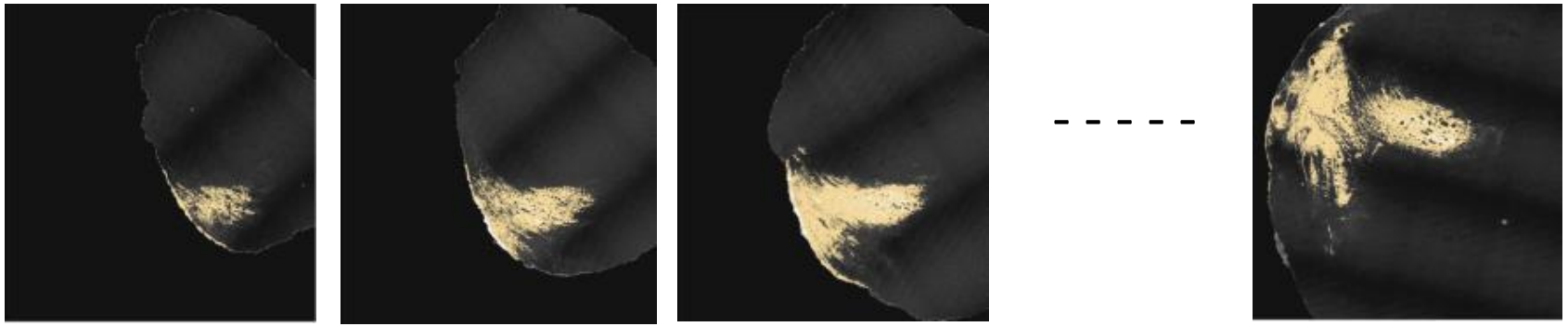


- 20 sections (layers)
- Spacing = 245 µm
- Total thickness = 4.9 mm

# Injectate Reconstruction

**2D masks for gel segmentation**



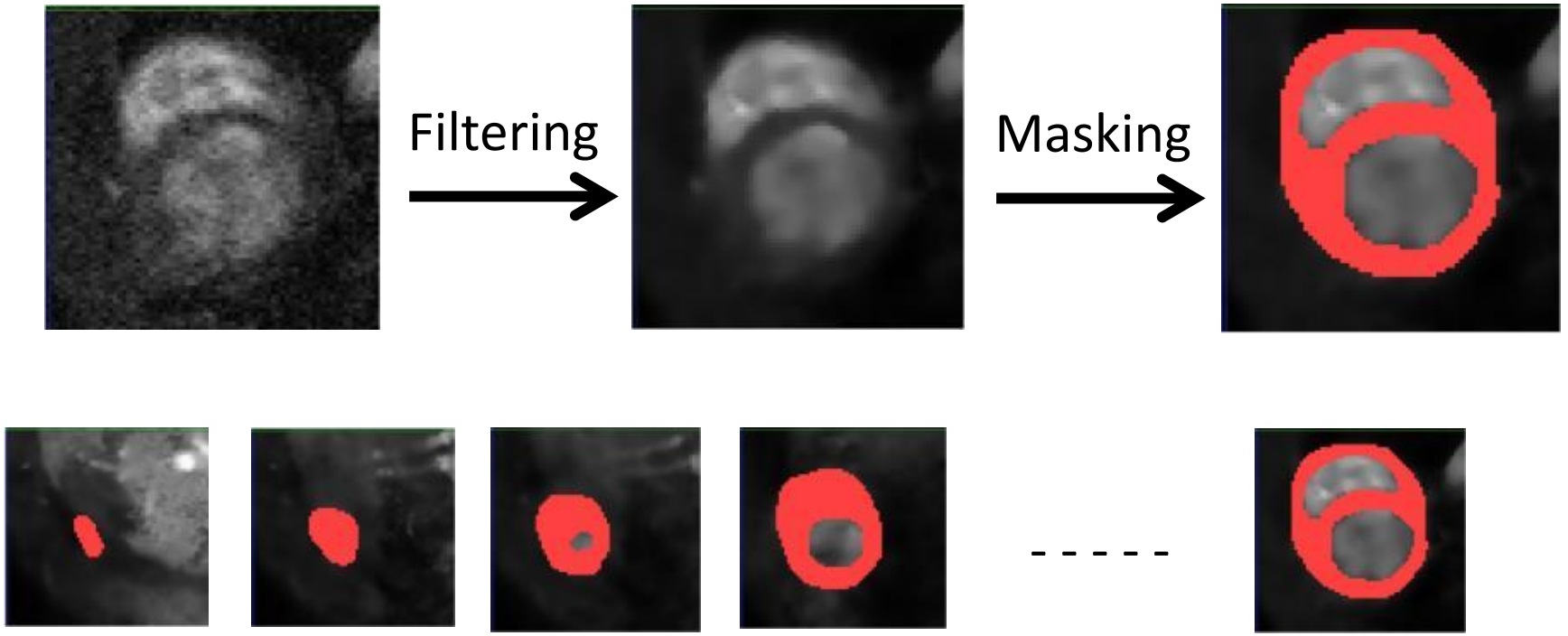
L1 L2 L3 L20

**3D geometry from reconstruction of 2D masks**

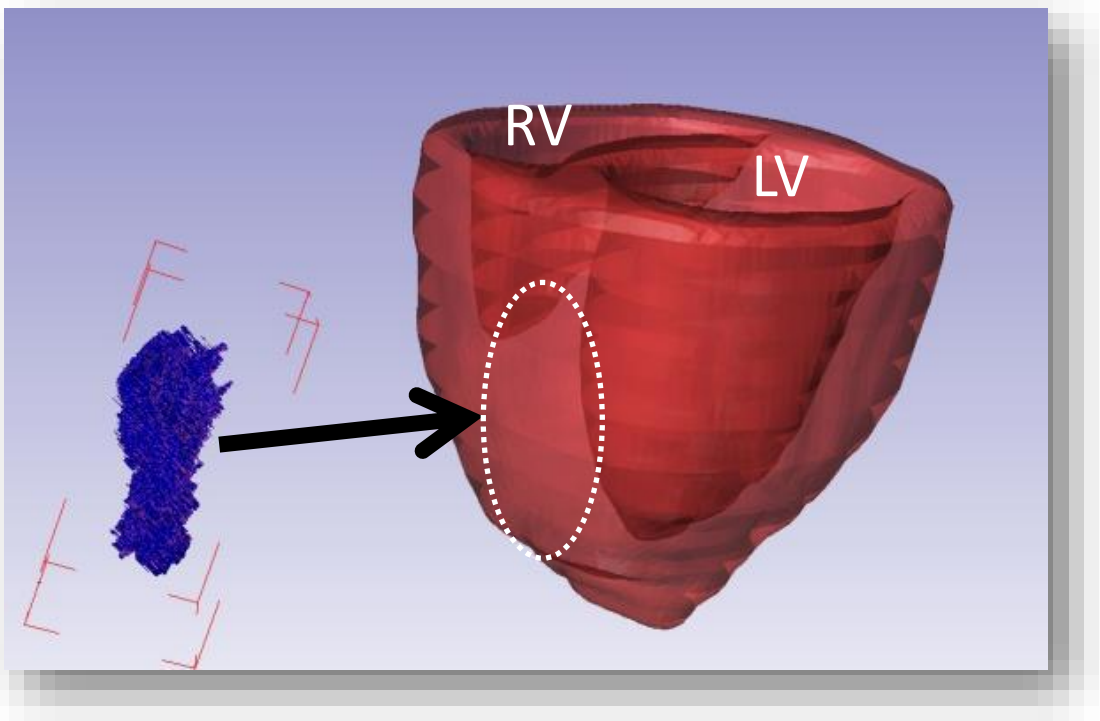
(Simpleware)

# Cardiac Reconstruction

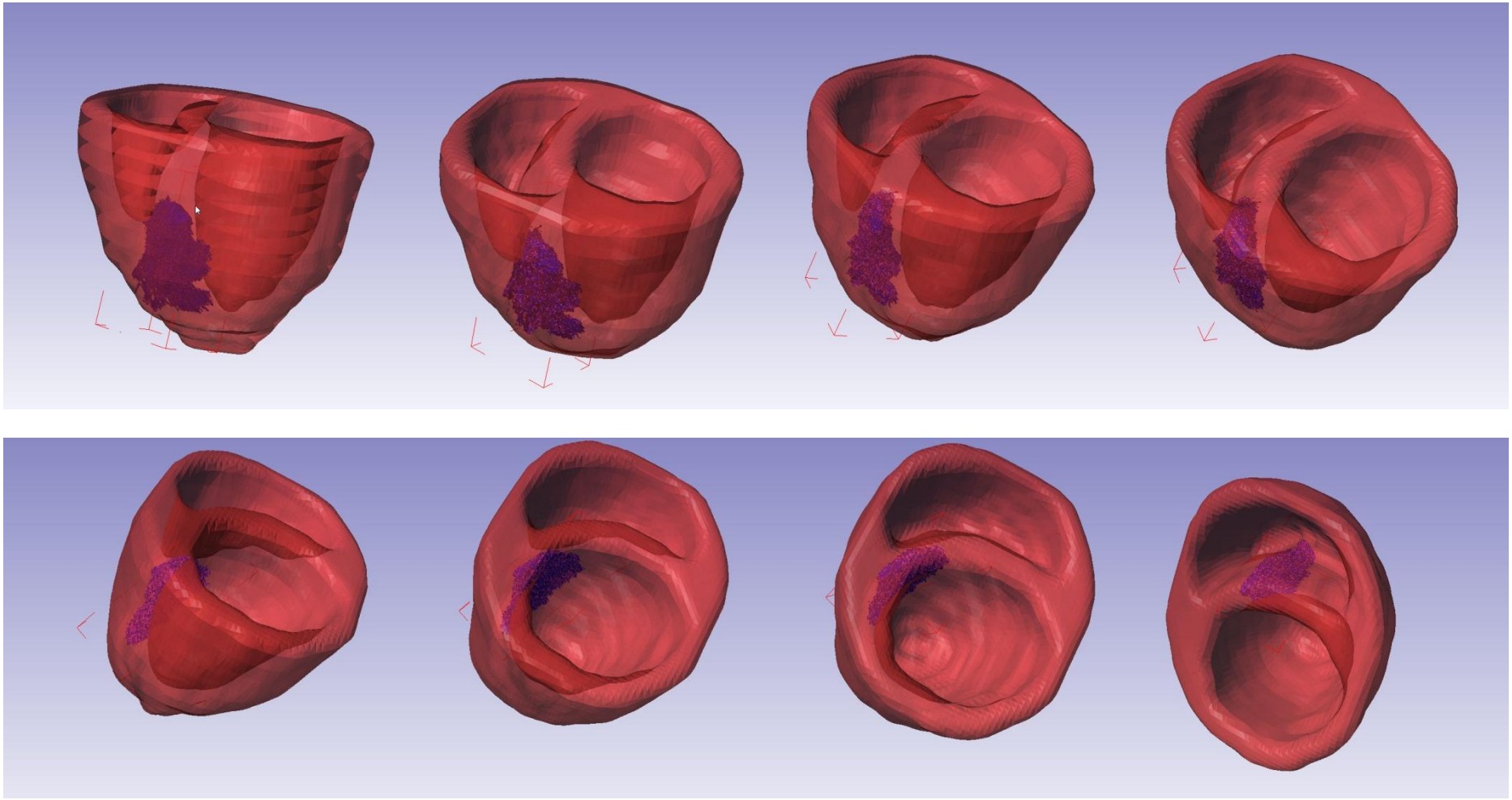
- Short-axis cardiac MRI of healthy rat
- 3T MRI system with custom small-animal bird cage coil



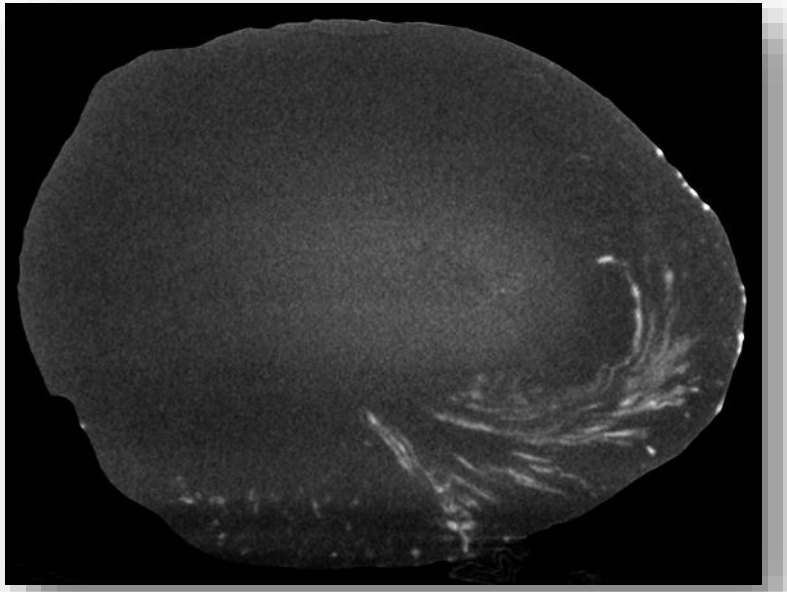
# Cardiac and Injectate Geometry

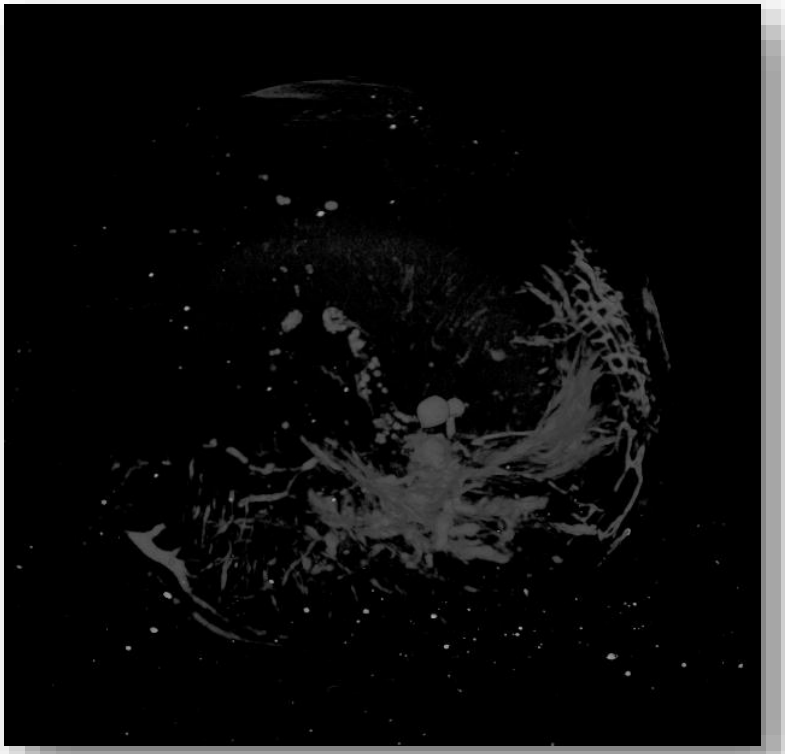


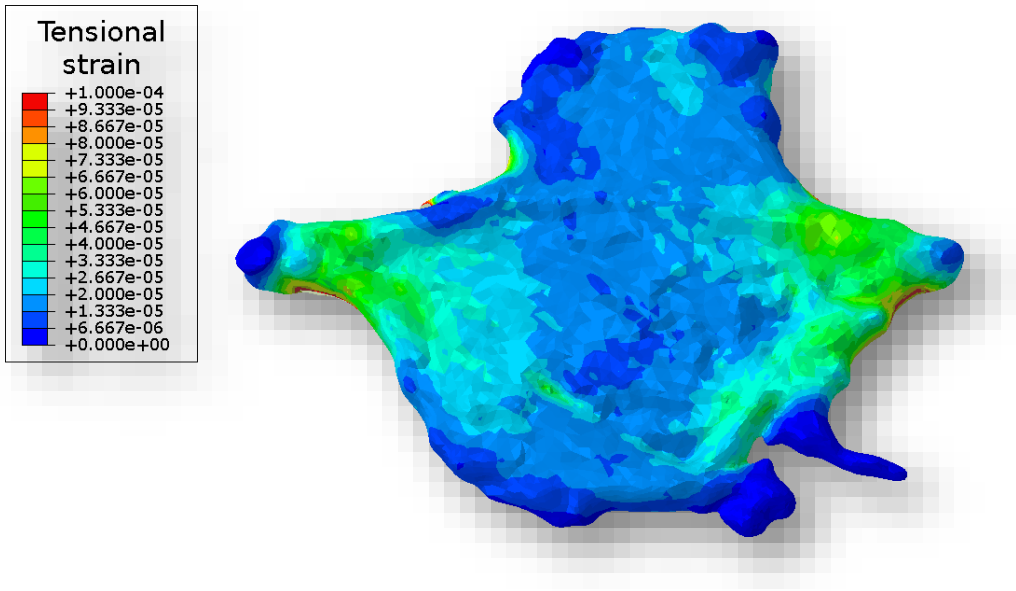
# Cardiac Geometry with Injectate



# µCT Injectate Imaging

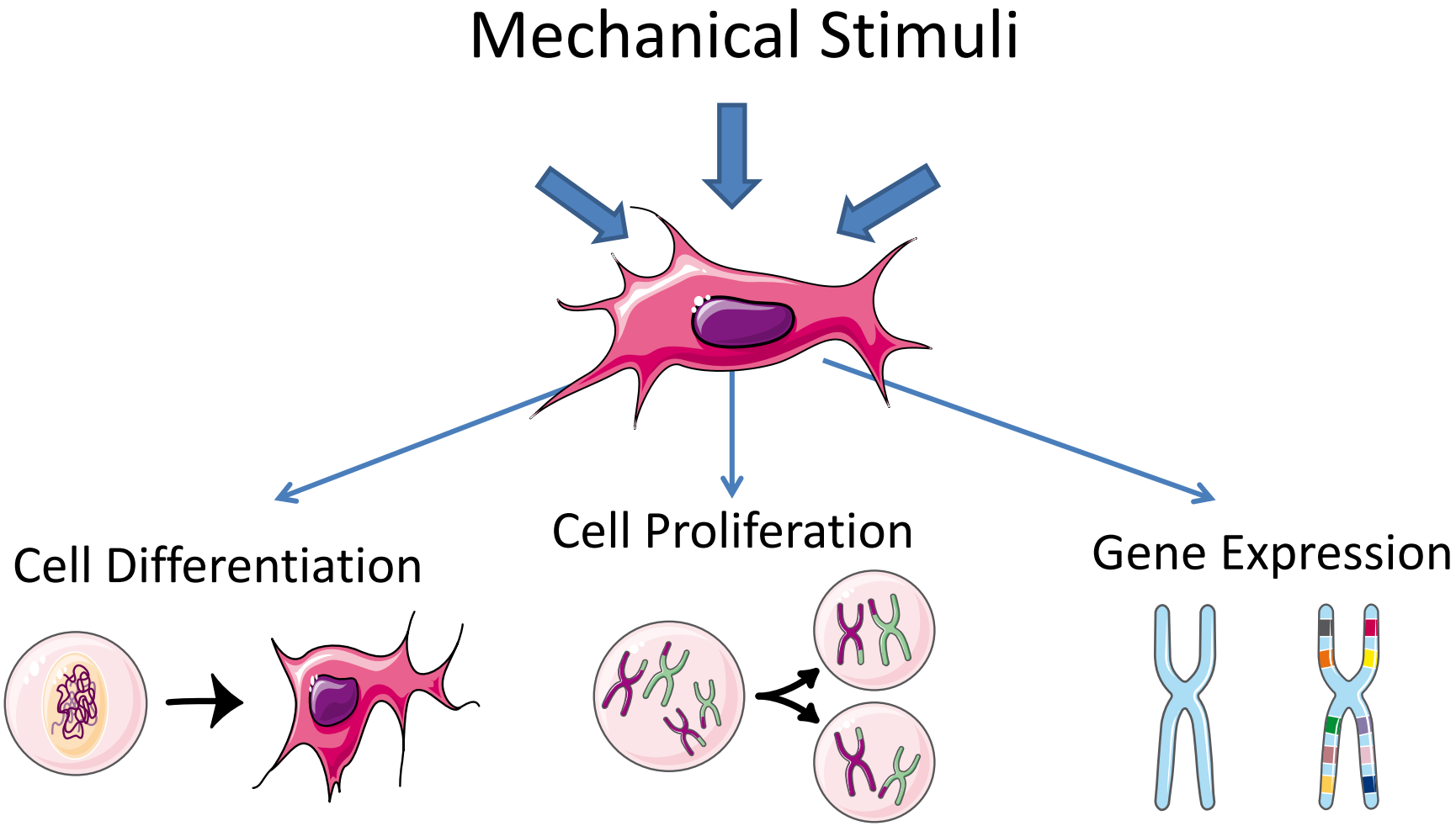




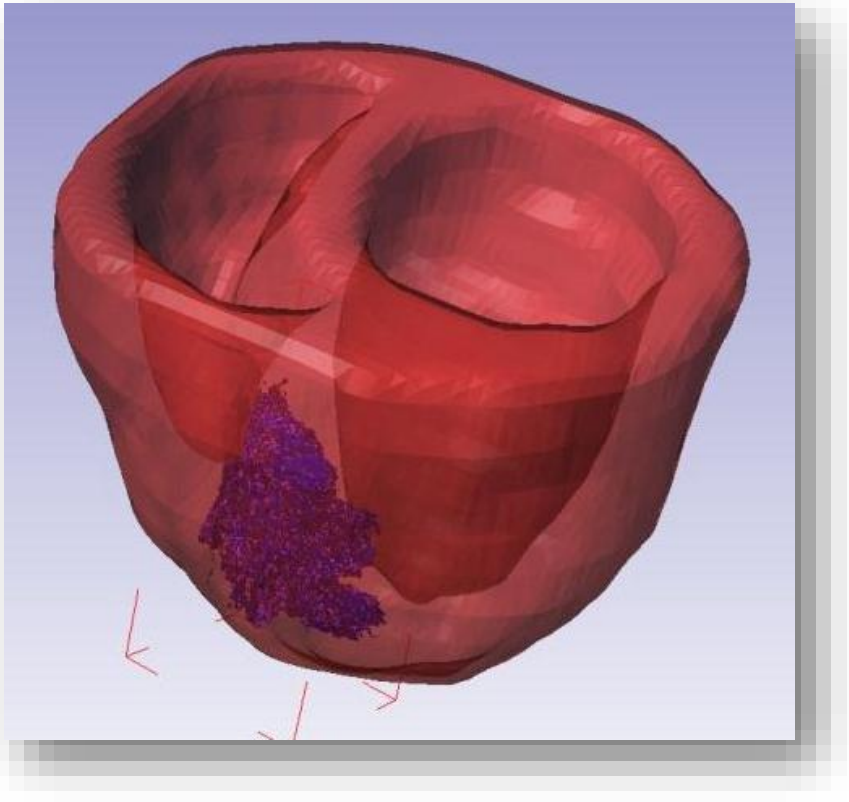



# CELL MECHANICS AND MECHANOBIOLOGY

# Mechanobiology

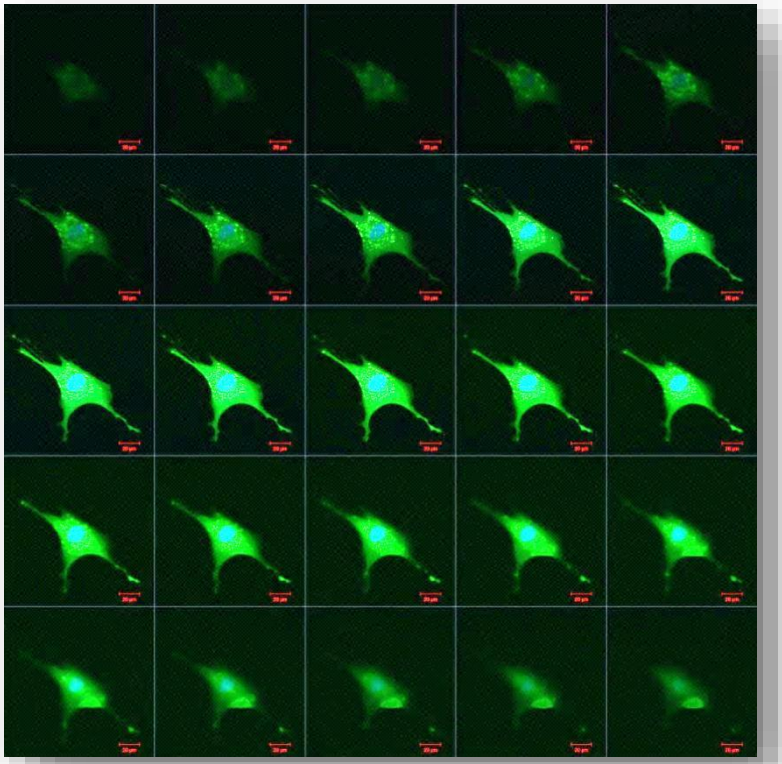


# Cell Therapies for Infarcted Hearts



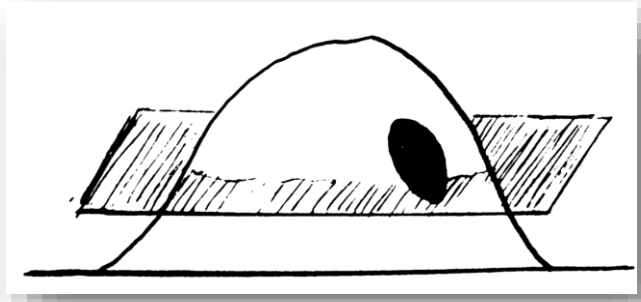
# Cell-specific Geometrical Modelling

Confocal microscopy images

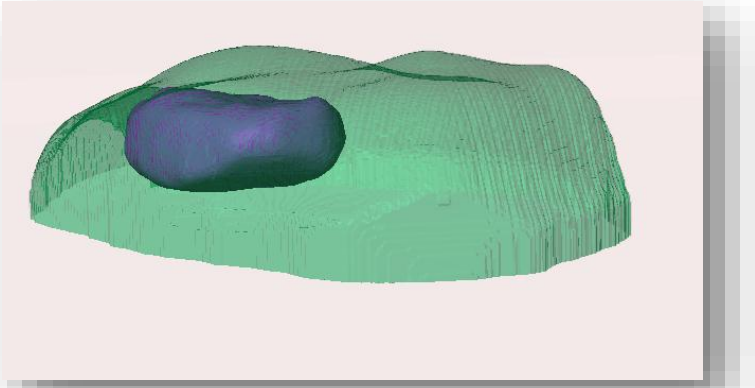


(Lancee, Davies, Dubuis, Franz)

Slicing through sample



3D Cell geometry



# Cell-specific Finite Element Model

Step 1: **Contact initiation**

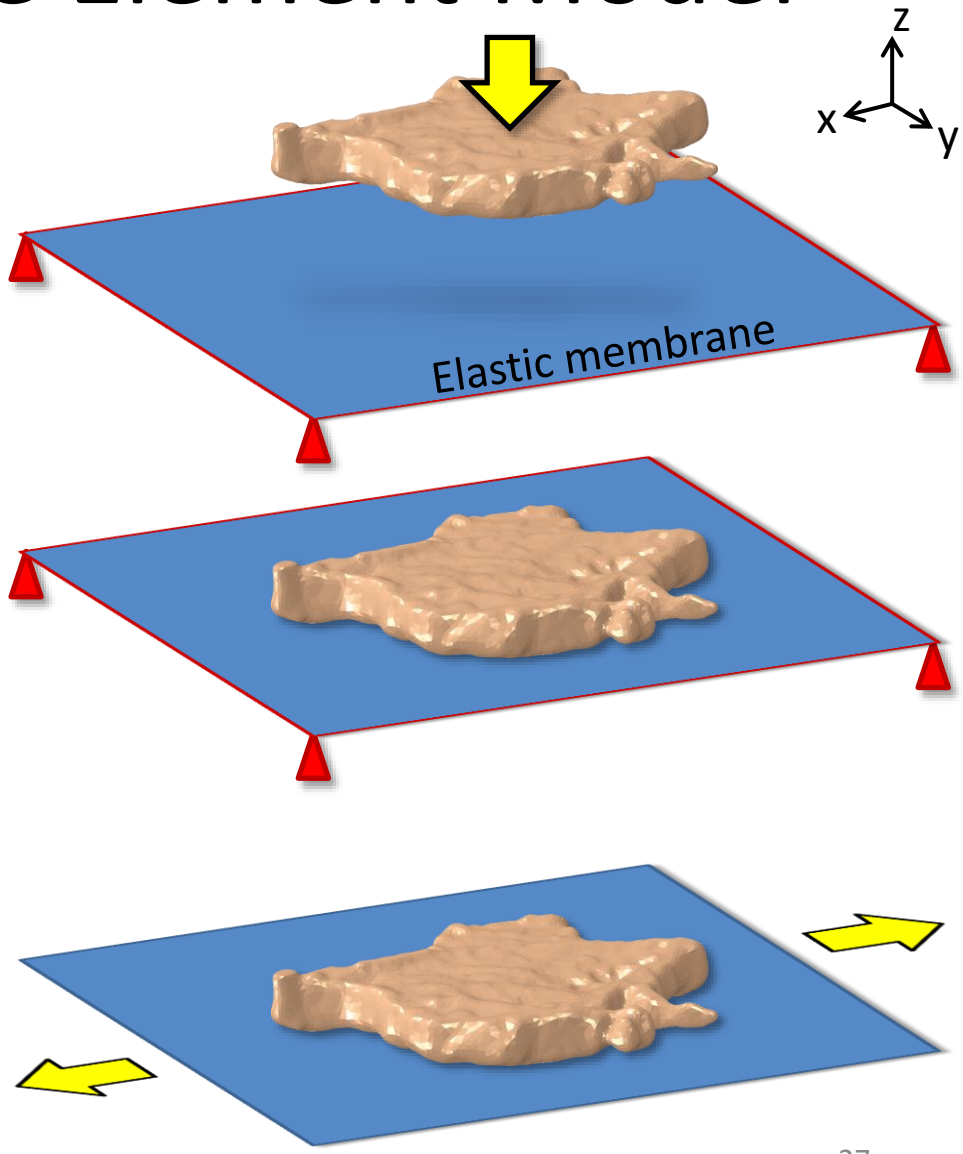
- Cell: vertical displacement till contact
- Membrane: fixed at its boundaries

Step 2: **Tie constraint**

- Cell: glued to the membrane at the FAs
- Membrane: fixed at its boundaries

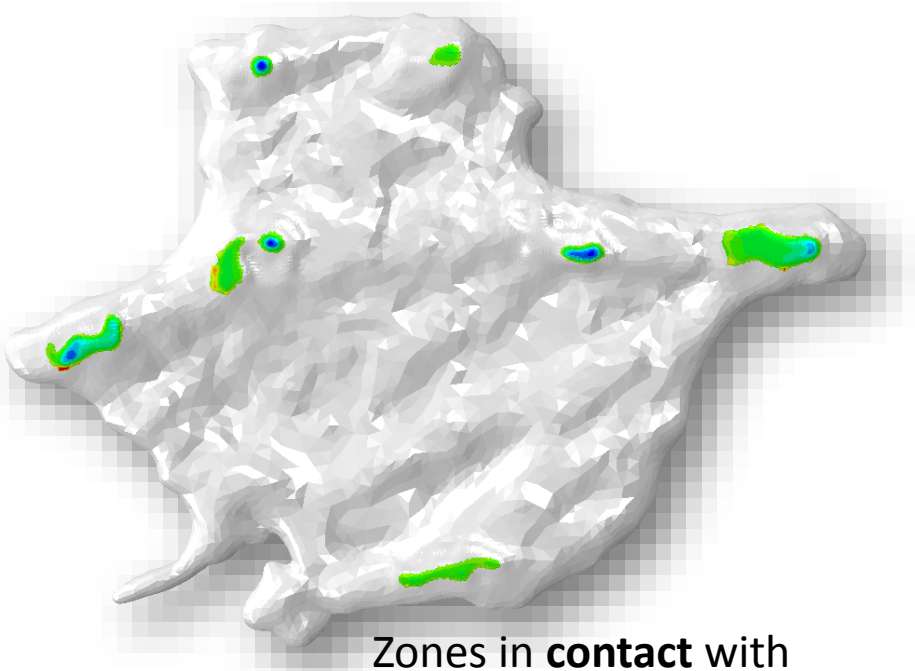
Step 3: **Stretching**

- Cell: glued to the membrane at the FAs
- Membrane: stretched along the x axis



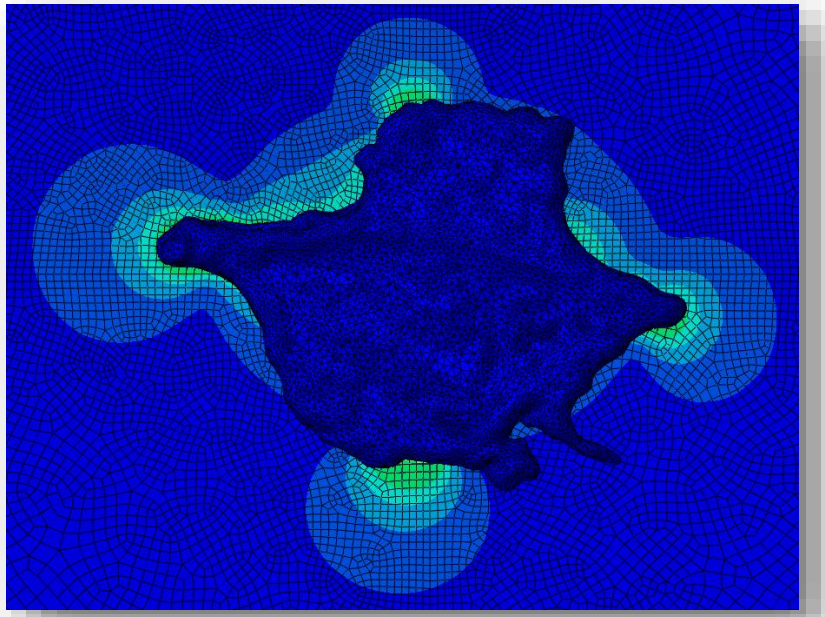
# Cell-specific Finite Element Model

Qualitative results of the focal adhesions



Zones in **contact** with the elastic substrate (bottom view)

Stress in Substrate



# Cell-specific Finite Element Model

Tensile **strain** (maximal principal strain)