# Multiscale Analysis Of Tissue Remodelling In Ascending Aortic Aneurysms

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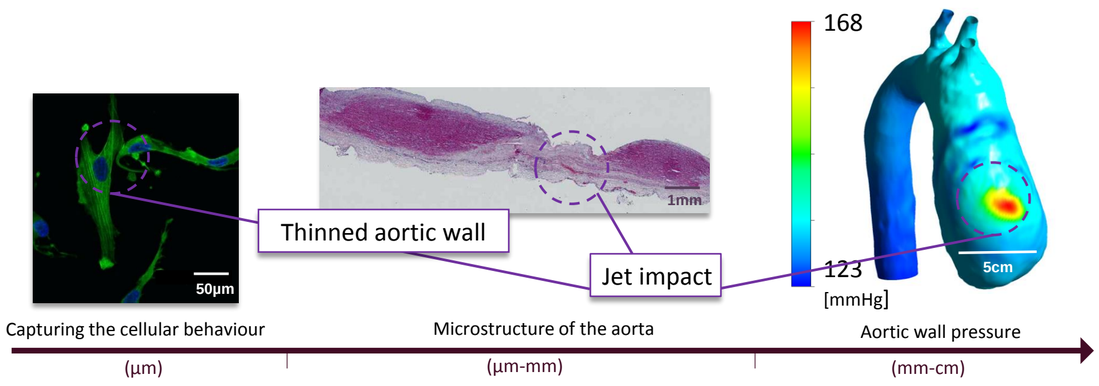
## Overarching Aim

Thoracic aortic aneurysms (TAA) increase the risk of aortic dissection or rupture and represent an important source of morbidity and mortality [1]. The exact mechanism behind them is still unclear.
The main aim of this study is to investigate the role of mechanical stimuli in the remodelling of arterial wall during the development of TAAs with the aim of developing a multiscale model by integrating the biomechanical environment of the aorta with cellular mechanics for predicting the vessel wall pathophysiology [2].

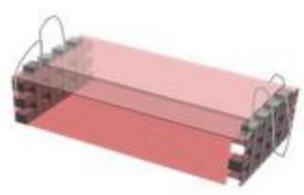
## Background

The effect of mechanical stimuli (such as blood pressure, hemodynamic shear stress and wall tensile stress) via mechanic-response of the cells in the wall have been considered significant in the development of TAAs, but the detailed underlying mechanism is yet to be elucidated.
Tissue engineered construct experiments are used as a starting point for establishing our multiscale framework for modelling mechanically-induced responses of fibroblasts and smooth muscle cells observed in vitro.

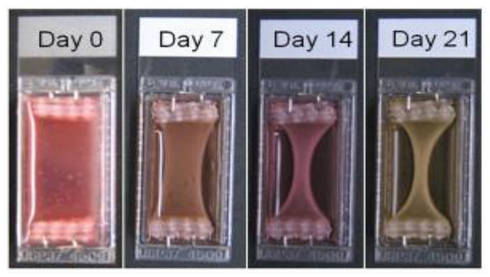



## In-Vitro data

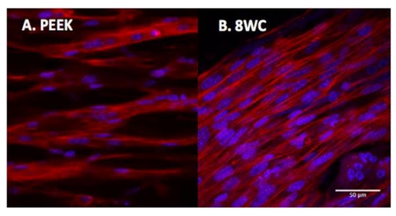
3D biomimetic hydrogel model promoting differentiation of C2C12 myoblasts into aligned multinucleated myotubes.



*In-vitro results[2],[4]*



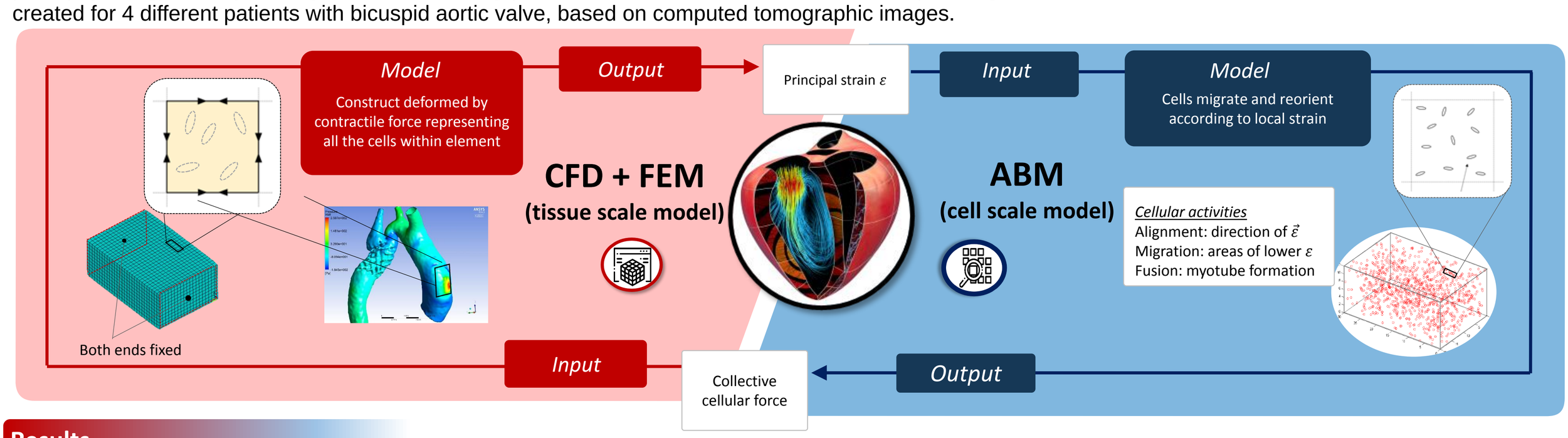

Construct deformation observational analysis over the course of the experiment (0, 4, 7, and 14 days).




Confocal images of formed myotubes within collagen matrix at 14 days.

## Methodology Overview

Multiscale computational framework to model the mechano-biological tissue-cell interaction in 3D in-vitro models of skeletal muscle for predicting the vessel wall pathophysiology and optimising the manufacturing process of muscular constructs. Patient-specific geometric models of the aortic arch and aortic root were created for 4 different patients with bicuspid aortic valve, based on computed tomographic images.




## Results

The tissue-scale model predicts the bowing deformation of the construct due to contraction of myocytes/myotubes, similarly to in vitro observations. In the cellular scale, the initially randomly oriented cells aligned approximately in the longitudinal direction of the construct, following the strain pattern in the construct[3]. The aorta of 4 patients with aortic disease (bicuspid aortic valve) is modelled to quantify the mechanical stimuli applied to the wall tissue to predict the cellular response.

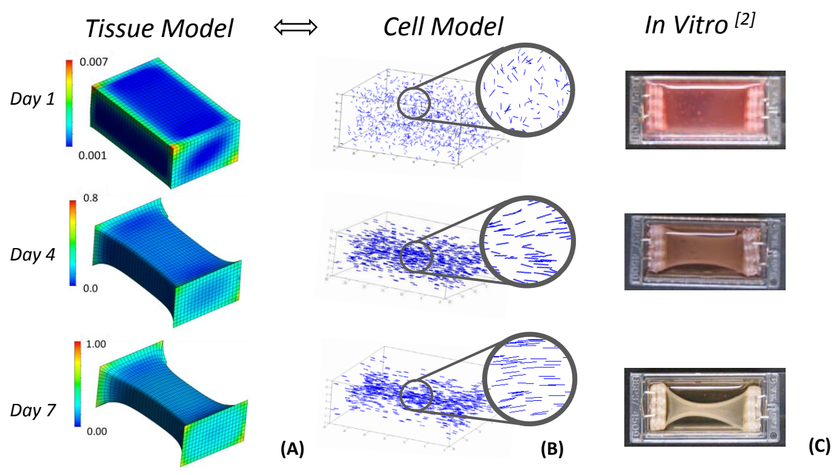



**Figure 1**: In silico model results in comparison to in vitro construct development. FEM results show total displacement and magnitude of principal strain (red-high and blue-low) and ABM results in show location as well as orientation of the cells by arrows.

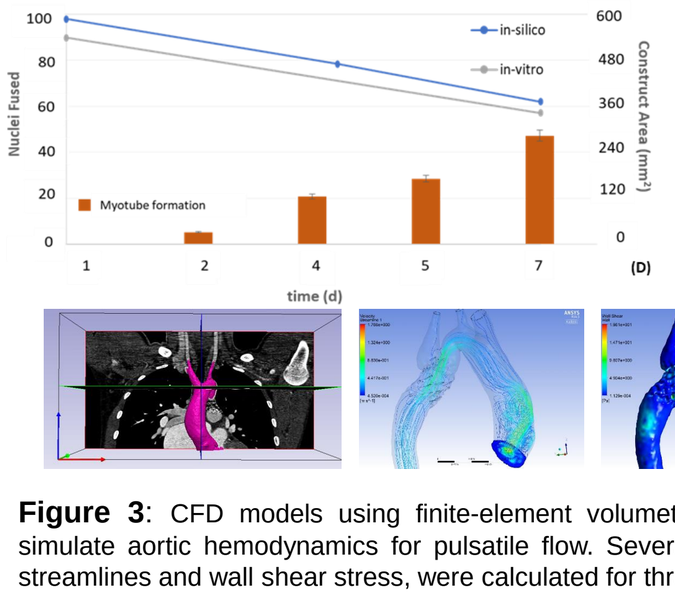



**Figure 2:** Graph of the computed maximum construct deformation (YX-plane) compared to in vitro data over a 7 day period. Histogram shows the cell nuclei fusion for myotube formation over a period of 7 days compared to the available in vitro observation at day 14[2].

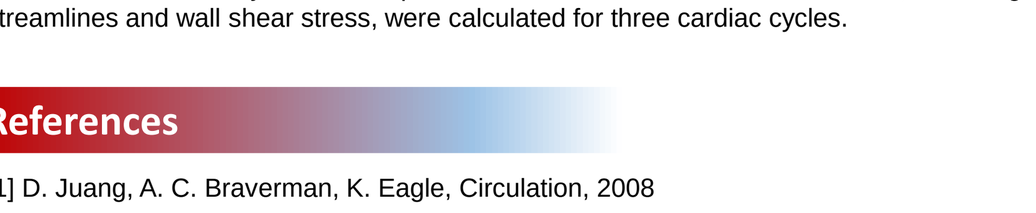


**Figure 3**: CFD models using finite-element volumetric meshing methods were used to simulate aortic hemodynamics for pulsatile flow. Several flow characteristics, including flow streamlines and wall shear stress, were calculated for three cardiac cycles.

## Conclusions

It has been demonstrated that the multi-scale model reproduces the overall construct development observed in vitro. Such approach fills the gap in experimentally acquired data and can be used to improve efficiency as well as functionality of tissue-engineered constructs. The multi-scale model when applied for modelling the aorta of patients with aortic disease can serving as a tool for predictive medicine answering clinical questions such as "which patient is at risk" & "when to intervene".

## References

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