digitalhealth REWIRED BIRMINGHAM 12-13 MARCH 2024

Headline Sponsors:

Graphnet Transforming Care

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WAHBI EL-BOURI

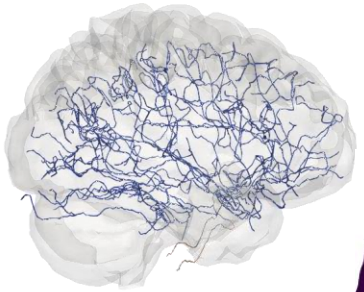
LECTURER IN DIGITAL TWINS, UNIVERSITY OF LIVERPOOL

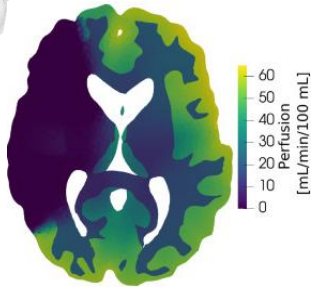
AI, DATA AND ANALYTICS STAGE

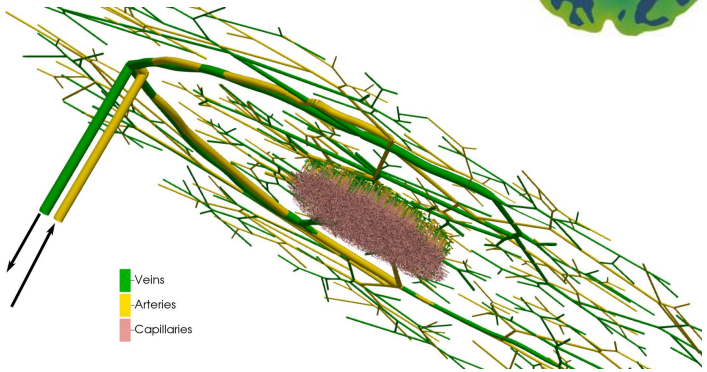
Stage Sponsor:

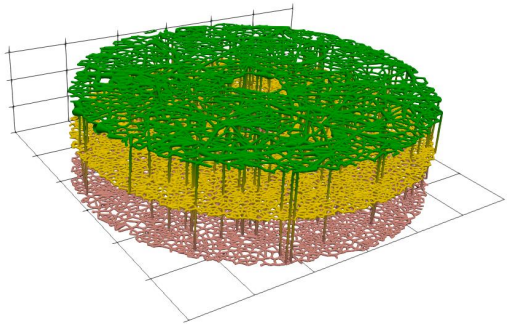
InterSystems Creative data technology

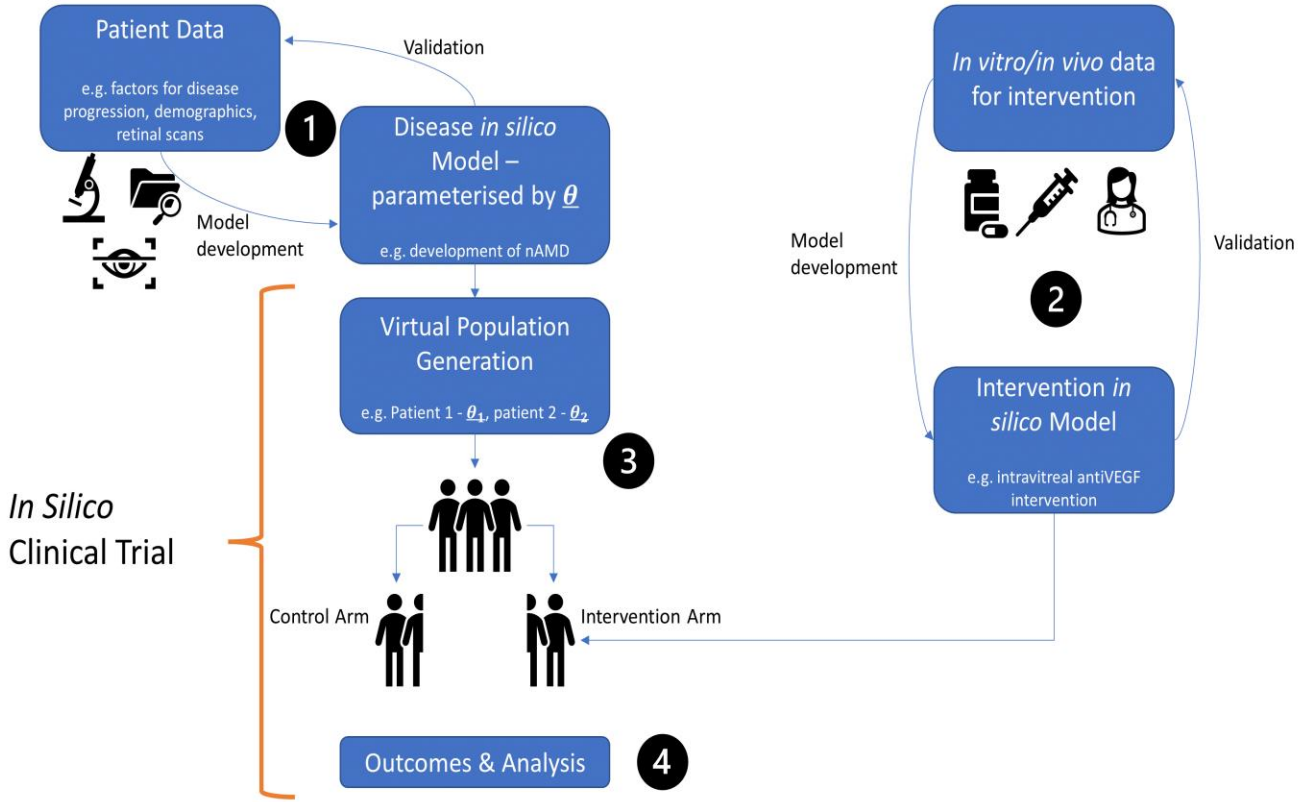
Digital twins in clinical trials











Hernandez et al., Progress in Biomedical Engineering, 2023

VIRTUAL VASCULAR HUMAN

About me and my group

- 3 years into Lectureshi
- Postdoctoral research
  Southampton General
- PhD in biomedical eng
  UOxf

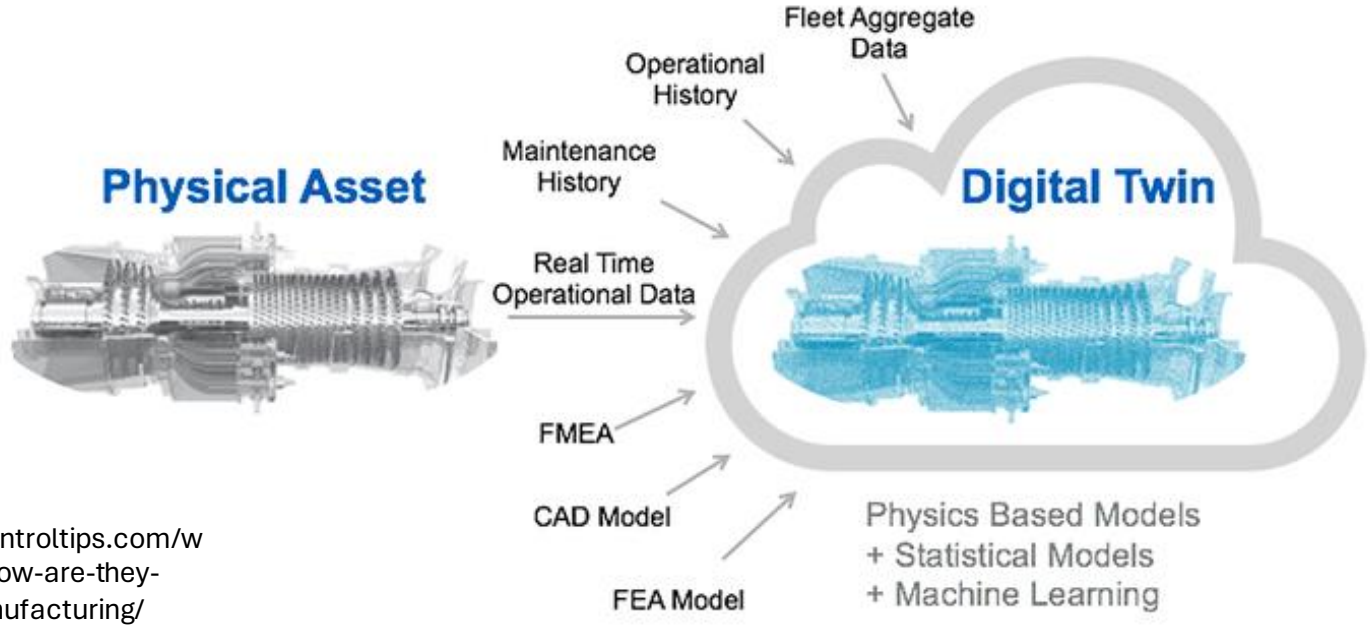
Key Points

1. There is more than one ‘type’ of digital twin

2. *In silico* clinical trials will **not** replace real-world clinical trials

What is a digital twin?

- A digital twin is a virtual model designed to accurately reflect a physical object
- Sensors attached to a real-world system inform a virtual environment where predictions can be made



https://www.motioncontroltips.com/what-are-digital-twins-how-are-they-used-in-industrial-manufacturing/

Types of Digital Twin

In healthcare, there are two main ‘types’ of digital twin:

1. Personalised Digital Twins

Personalised

For an individual

Unique

AccuCities

2. Digital Twins for *in silico* clinical trials

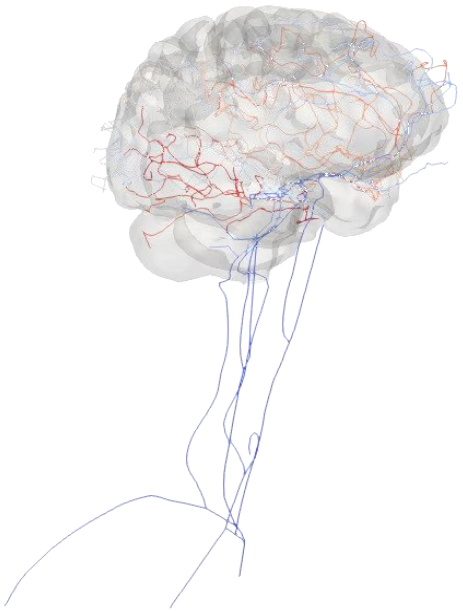
Represent the **average** of a population or group of people

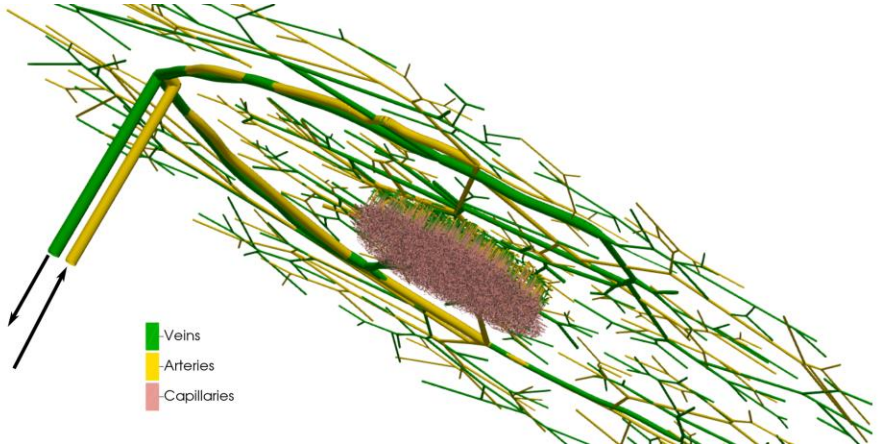
Not unique to an individual

Statistically correct

SmartCitiesWorld

Two examples

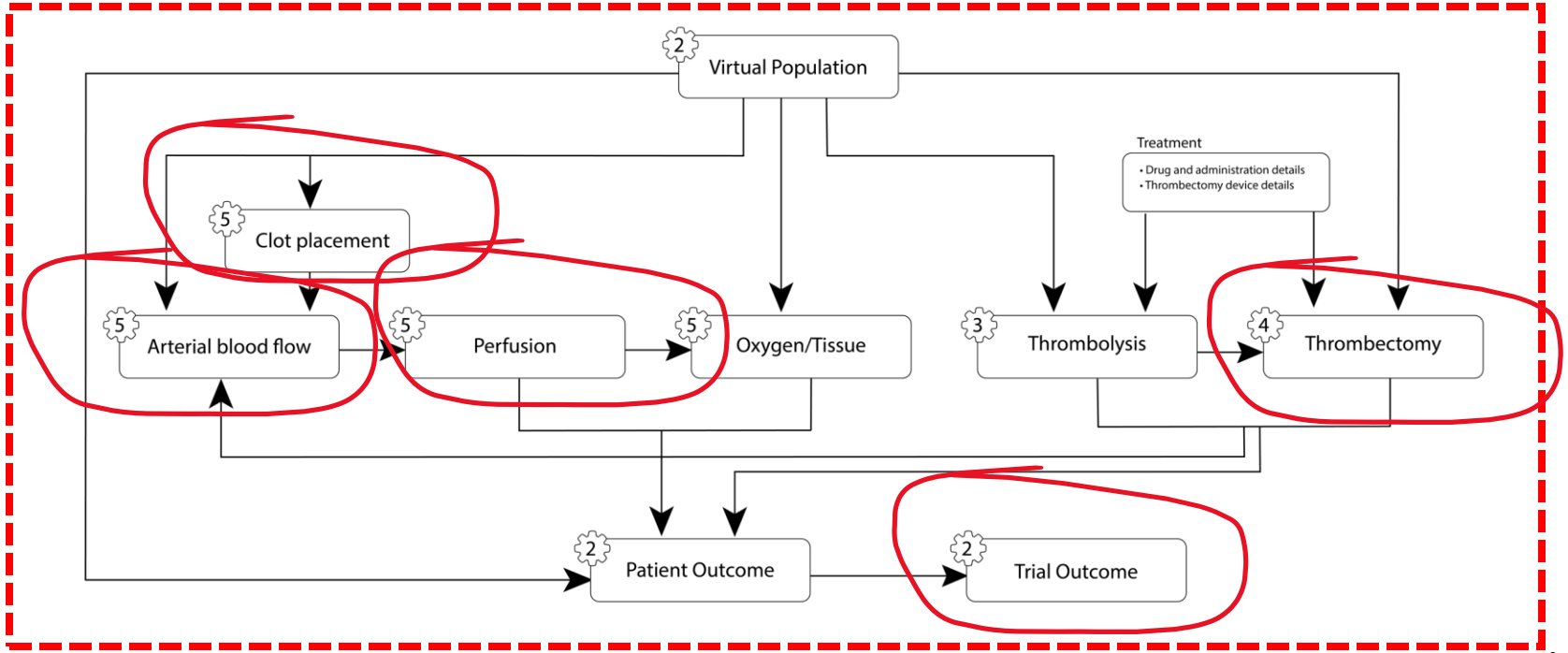




In silico clinical trials of ischaemic stroke

Input data

Model

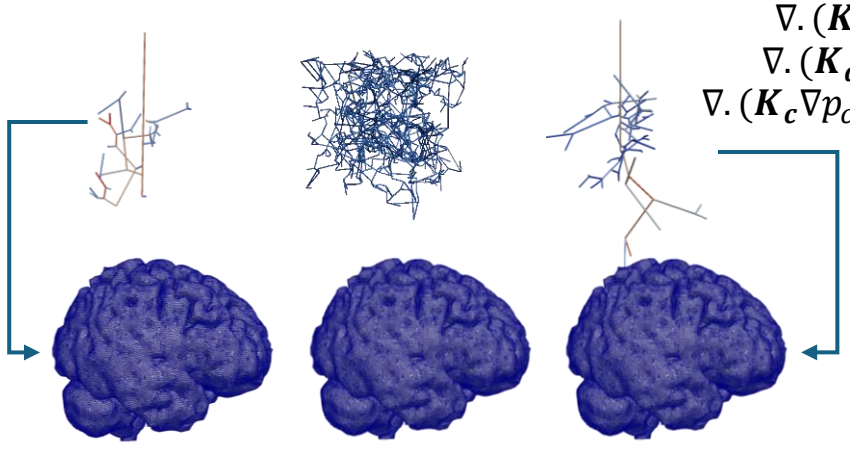


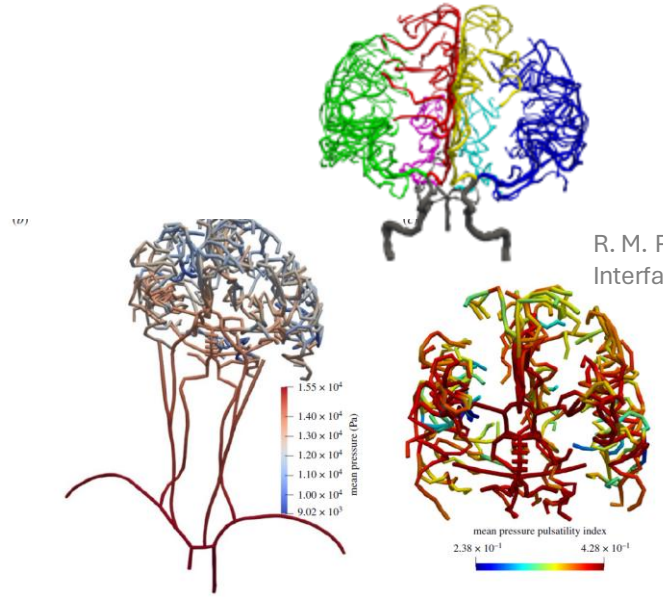
Outcomes: mRS; infarct volume

https://www.insist-h2020.eu/index.php/home/wp-6

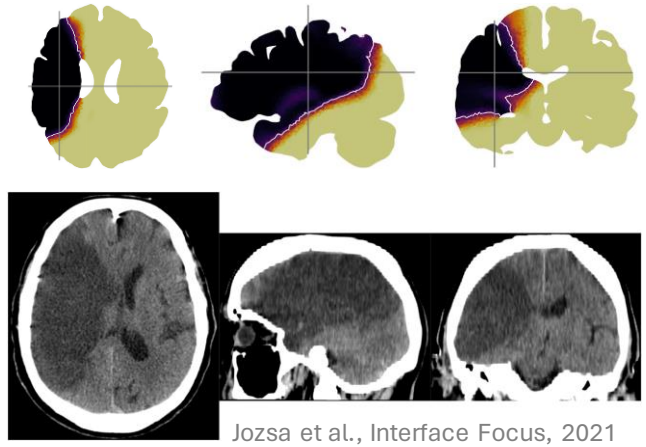
In silico clinical trial modules

$$\nabla.(\boldsymbol{K_v}\nabla p_v + \beta_{cv}(p_c - p_v) = 0$$
$$\nabla.(\boldsymbol{K_a}\nabla p_a) - \beta_{ac}(p_a - p_c) = 0$$
$$\nabla.(\boldsymbol{K_c}\nabla p_c) + \beta_{ac}(p_a - p_c) - \beta_{cv}(p_c - p_v) = 0$$

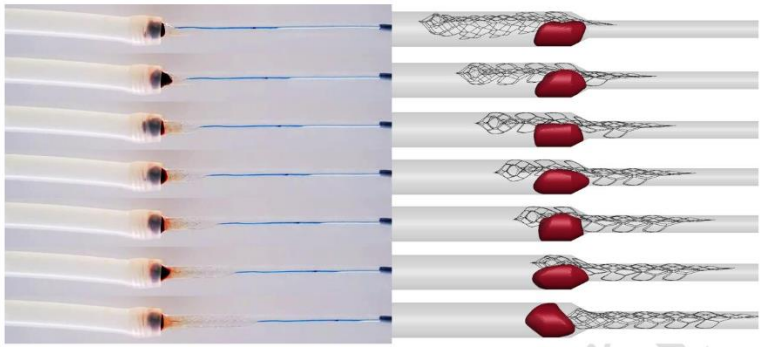




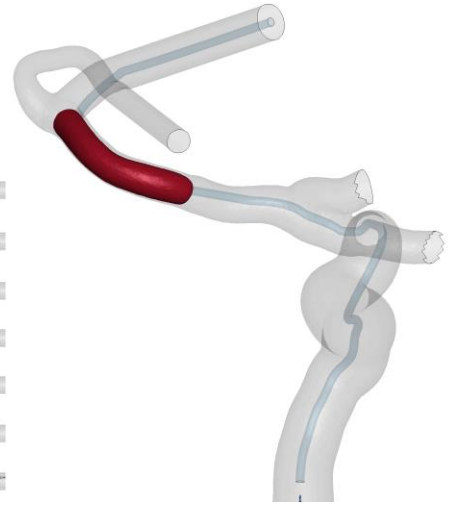
R. M. Padmos et al., Interface Focus 2021



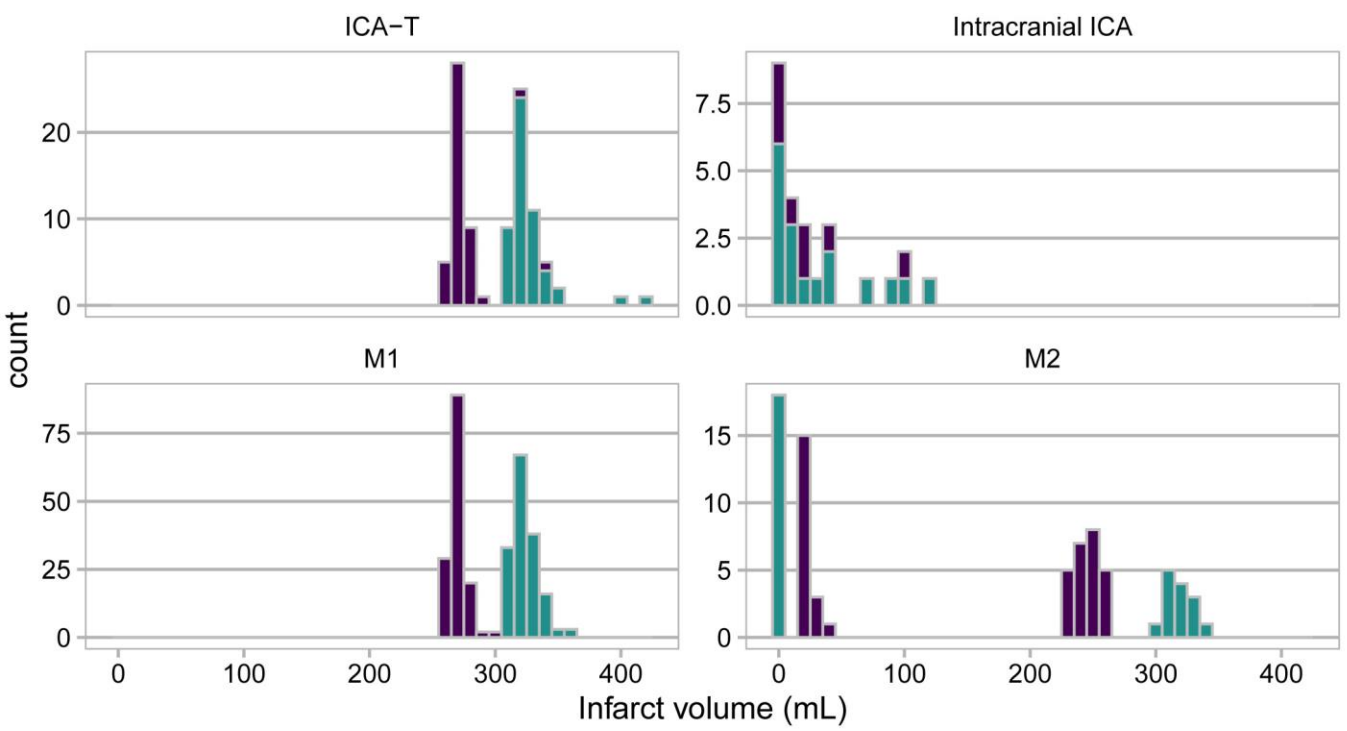
Jozsa et al., Interface Focus, 2021

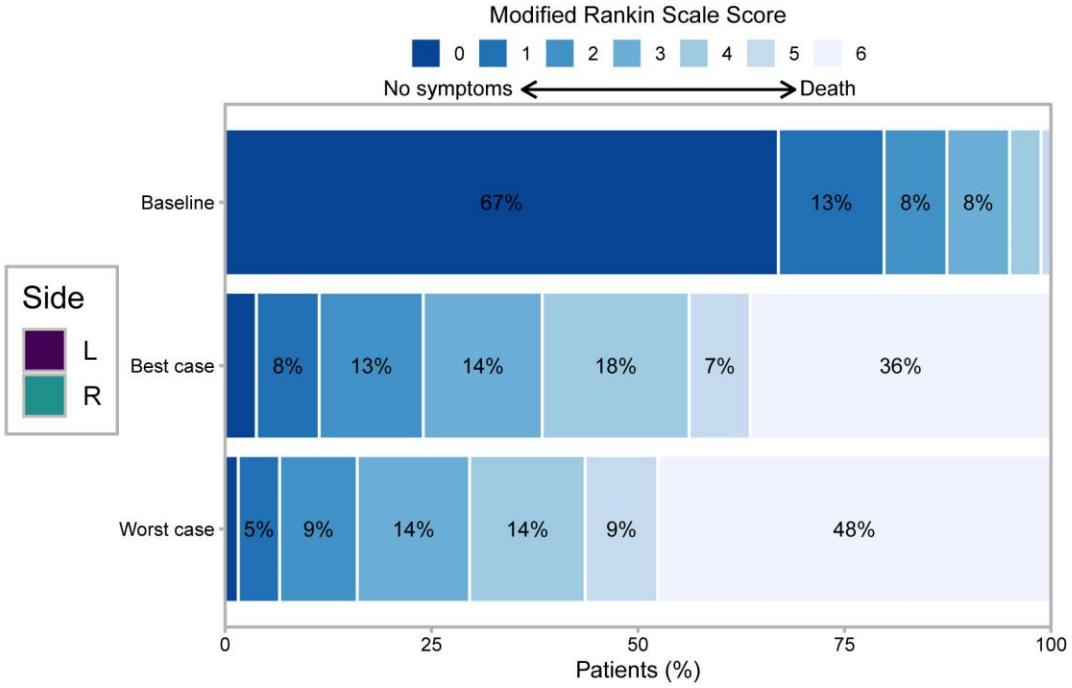


G. Luraghi et al., Interface Focus 11: 20190125 2021



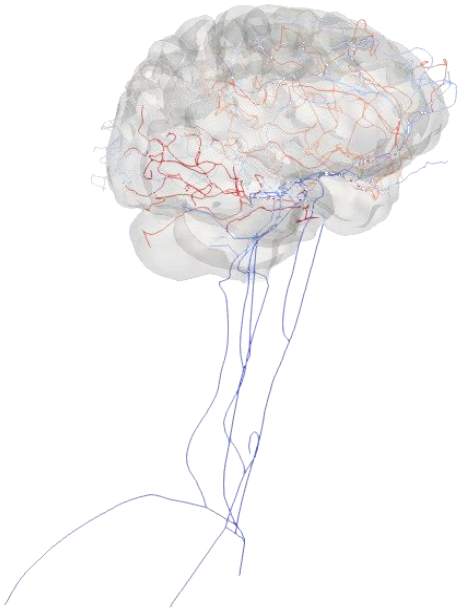
In silico clinical trial outcomes

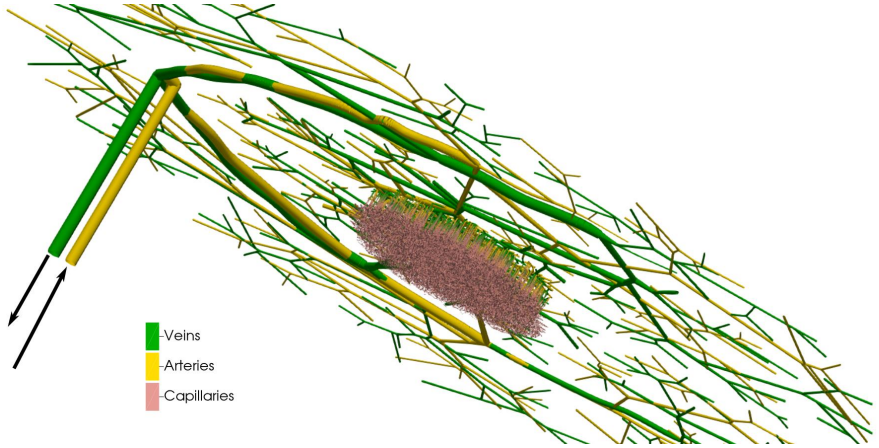




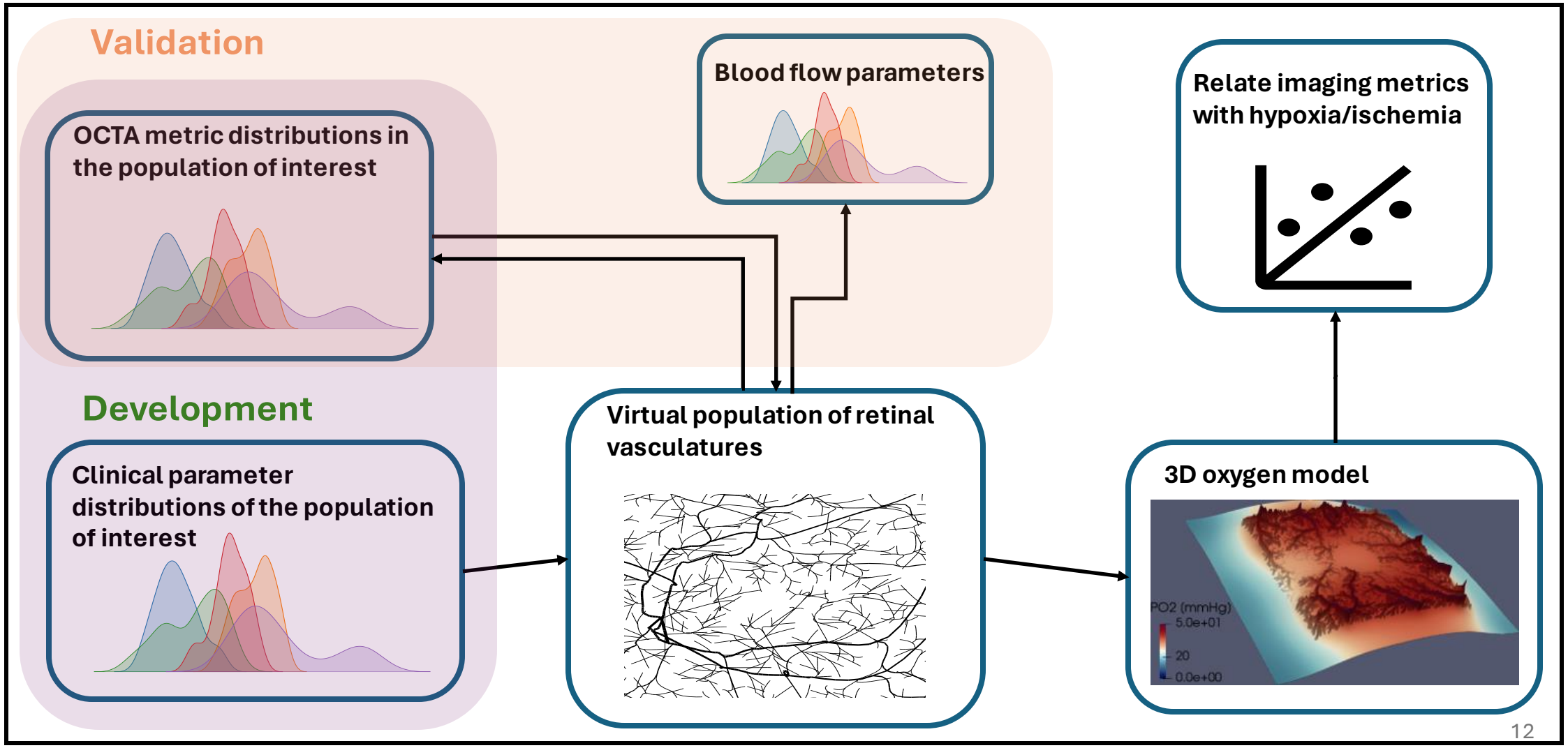
Miller et al., Comp. in Biol. & Med., 2021

Two examples



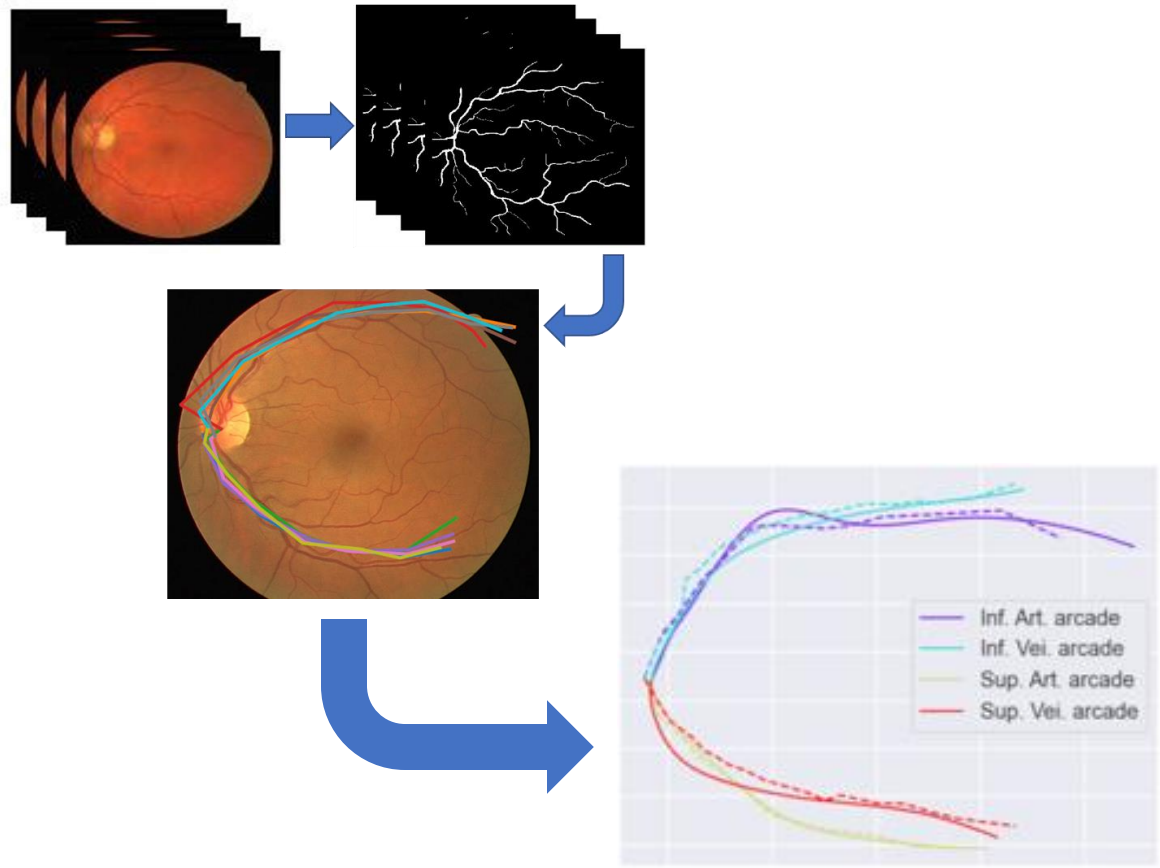


Digital Populations of the eye

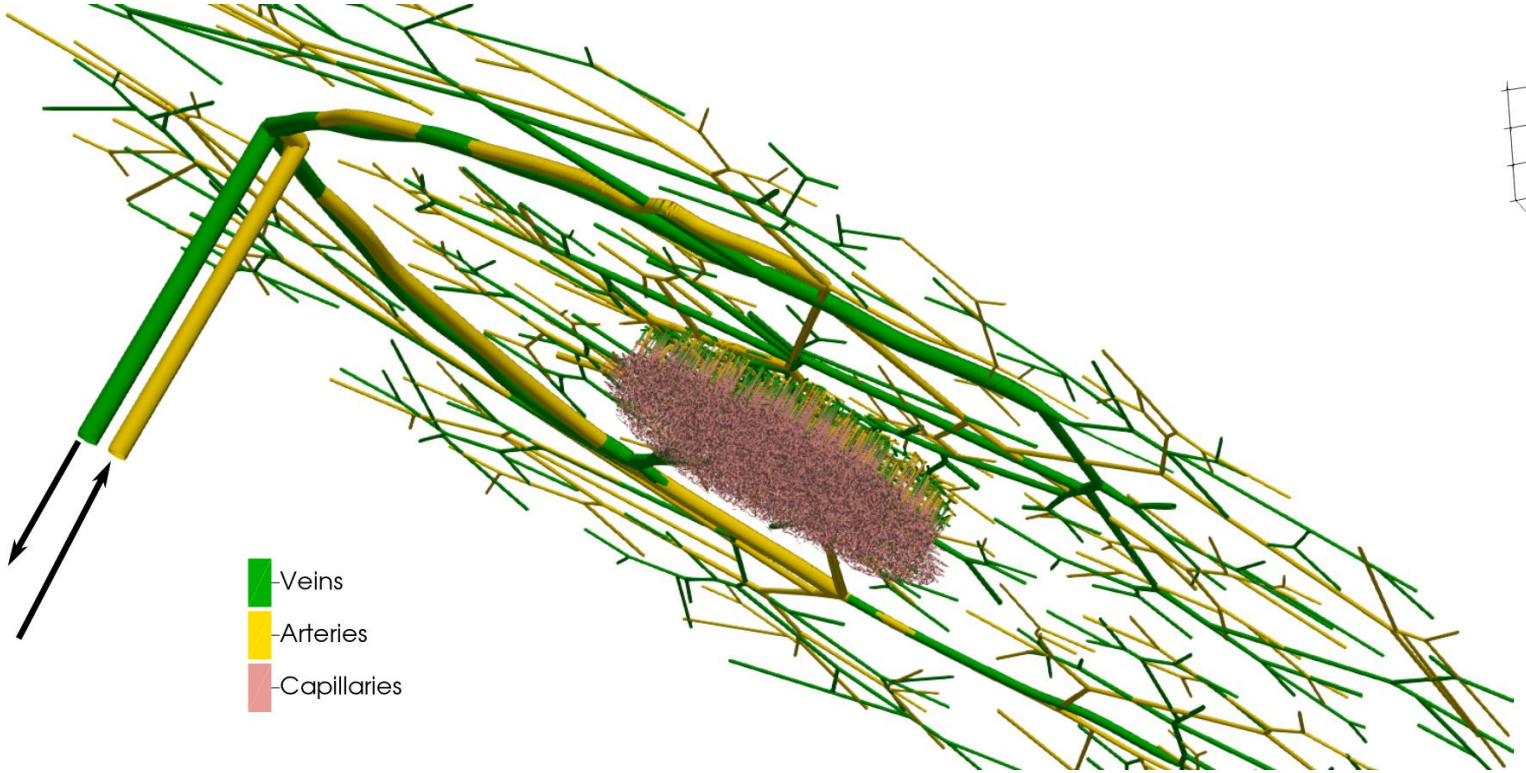


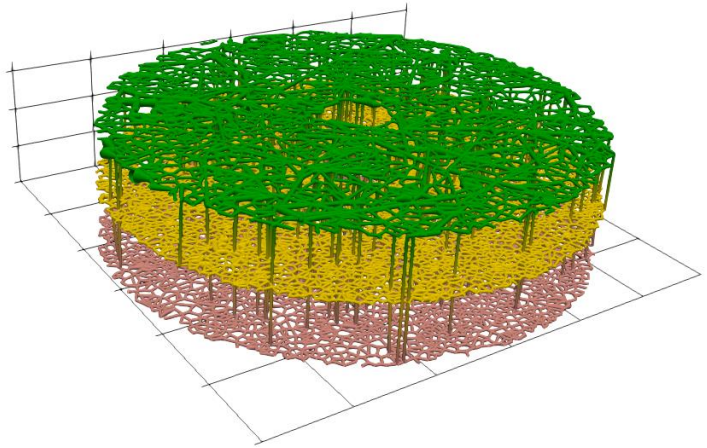
Statistical shape modelling

- Creating an image-based backbone
  1. Manual segmentation of the major retinal arcades
  2. Learn the position of inflection points of the arcades
  3. Align all shapes using SVD (‘Procrustes analysis’)
- Generate new shapes
  - $X = \bar{X} + P \cdot b$, with $b \sim \mathcal{N}(\mu, \sigma)$ and P the principal components’ direction



Digital Populations of the eye



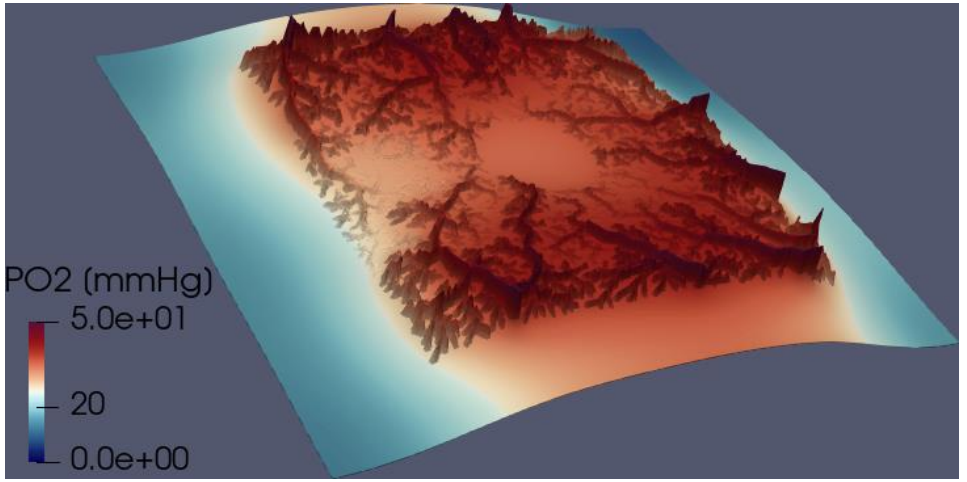


Hernandez et al., IOVS (under review), 2024

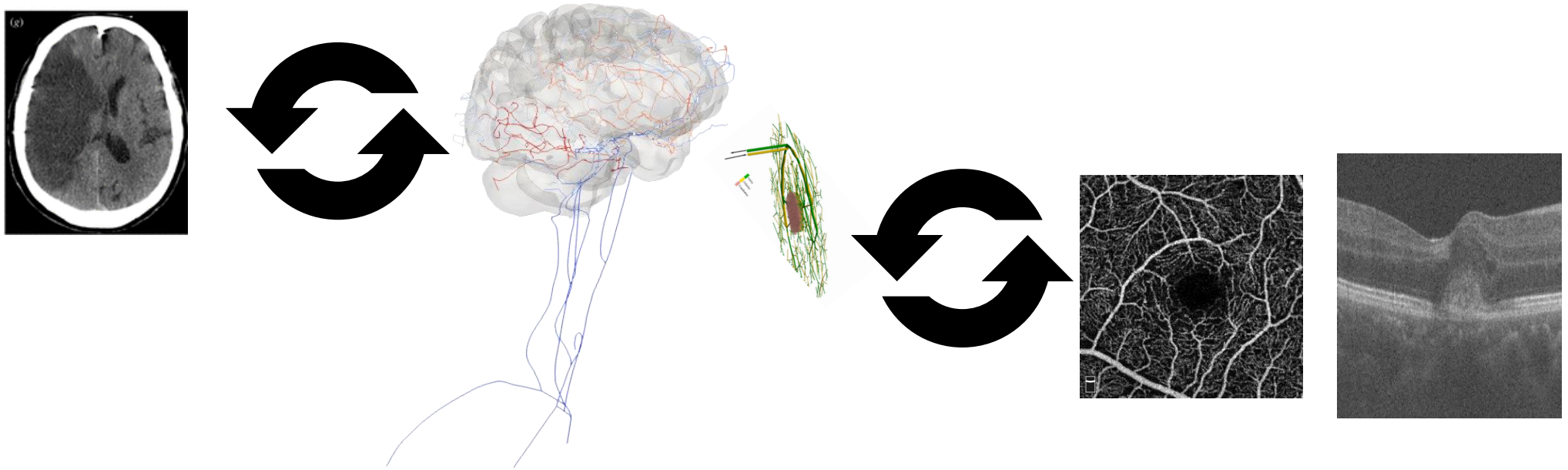
Simulating the disease

Develop a disease and treatment model so that we can run *in silico* clinical trials as well as determine personalised treatment responses.

$$\begin{cases} v \cdot \nabla c_{blood} = -\Gamma(c_{blood} - \mathrm{c}_{\mathrm{tissue}}) \\ \nabla \cdot (D \nabla c_{tissue}) + \Gamma(c_{blood} - c_{tissue}) - Q_{O_2} c_{tissue} = 0 \end{cases}$$



Building up *in silico* vascular digital twins



Continual improvement of the model with clinical data in turn drives what data will be required to further improve the model

Unknown unknowns…

“Reports that say that something hasn't happened are always interesting to me, because as we know, there are **known knowns**; there are things we know we know. We also know there are **known unknowns**; that is to say we know there are some things we do not know. But there are also **unknown unknowns**—the ones we don't know we don't know.” – Donald Rumsfeld

The **unknown unknowns** are not modelled – therefore will never appear in our *in silico* clinical trials

An example...

However…

- Digital twins can be used to augment real-world clinical trials reducing time and costs
- Excellent in prototyping medical devices in simulated real-world use cases
- Can test ‘edge’ or rare cases effectively
- Early successes seem to be in the pre-clinical and animal model testing phases

Key Points

1. There is more than one ‘type’ of digital twin

2. *In silico* clinical trials ~~will **not**~~ can replace real-world clinical trials [in some cases]

Key Points

3

Digital twin technology is rapidly developing and will revolutionise clinical trials and personalised healthcare

UNIVERSITY OF LIVERPOOL

Liverpool Centre for Cardiovascular Science

VIRTUAL VASCULAR HUMAN

Thanks for listening!

THE ROYAL SOCIETY

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