EDITH proof-of-concept infrastructure

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EDITH is a coordination and support action funded by the Digital Europe program of the European Commission under grant agreement n° 101083771

Outline of the session

- Presentation of application and related technical implementation

- User perspectives are used to guide presentation
    - researchers
    - communities
    - industry
    - clinicians
    - patients

Researchers

Caroline Roney or Laura Bevis, Elisa Rauseo, Queen Mary University of London

EDITH

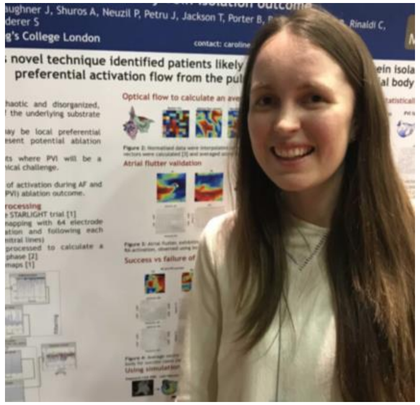
EDITH is a coordination and support action funded by the Digital Europe program of the European Commission under grant agreement n° 101083771

Cardiovascular Use Case: Personalised Models for Atrial Fibrillation

Dr Laura Bevis, Postdoctoral Research Associate (l.bevis@qmul.ac.uk)

Personalised Cardiac Modelling Lab (PCM Lab), Dr Caroline Roney (UKRI Future Leaders Fellow)
School of Engineering and Materials Science, Digital Environment Research Institute, QMUL

Who we are…



Dr Caroline Roney

UKRI Future Leaders Fellow
Reader in Computational Medicine

Mathematics, Biomedical Engineering, Computational Modelling

Dr Elisa Rauseo

Cardiologist with special interest in Cardiovascular imaging and AI

Queen Mary University of London, Barts Health NHS Trust

Dr Laura Bevis

Postdoctoral Research Associate in Cardiac Digital Twins

Mathematician - Fluid Dynamics, Biological Modelling

Prof Greg Slabaugh

Professor of Computer Vision and AI

Director of the Digital Environment Research Institute (DERI)

Personalized Cardiac Modelling Lab, School of Engineering and Materials Science, Queen Mary University of London

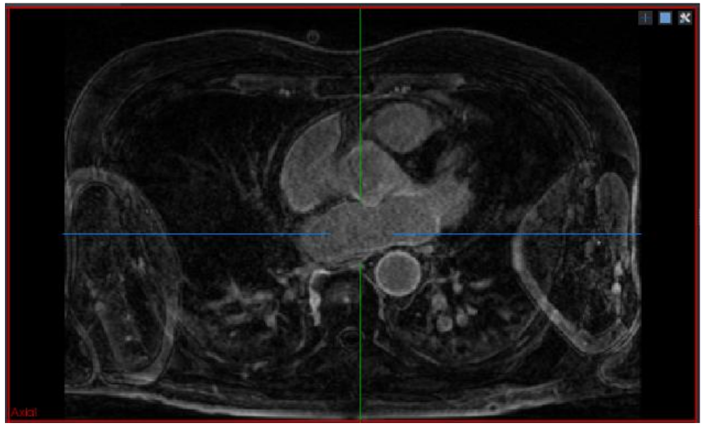
Digital Environment Research Institute, Queen Mary University of London

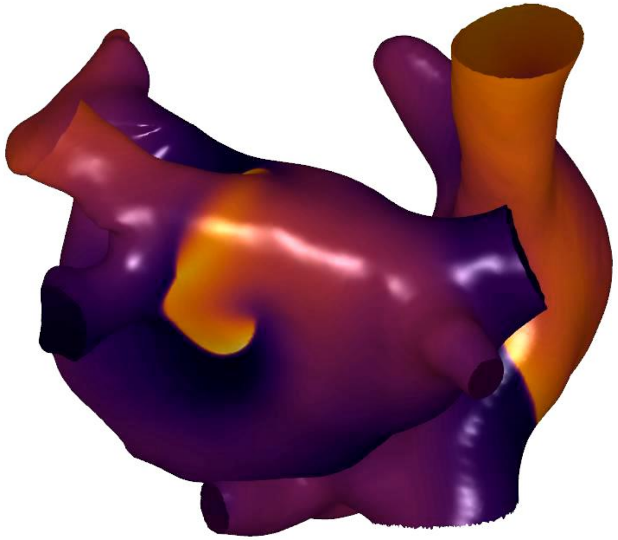
Plus clinical collaborators at Barts NHS Trust

Who we are…

QMUL Cardiovascular Use Case

- Personalised simulations for atrial fibrilation
  - **Inputs:** Patient specific anatomy from CT, MRI or electroanatomical mapping (EAM) data
  - **Outputs:** Patterns of electrical activity that indicate targets for personalised AF treatment
- Clinical collaboration to ensure relevance

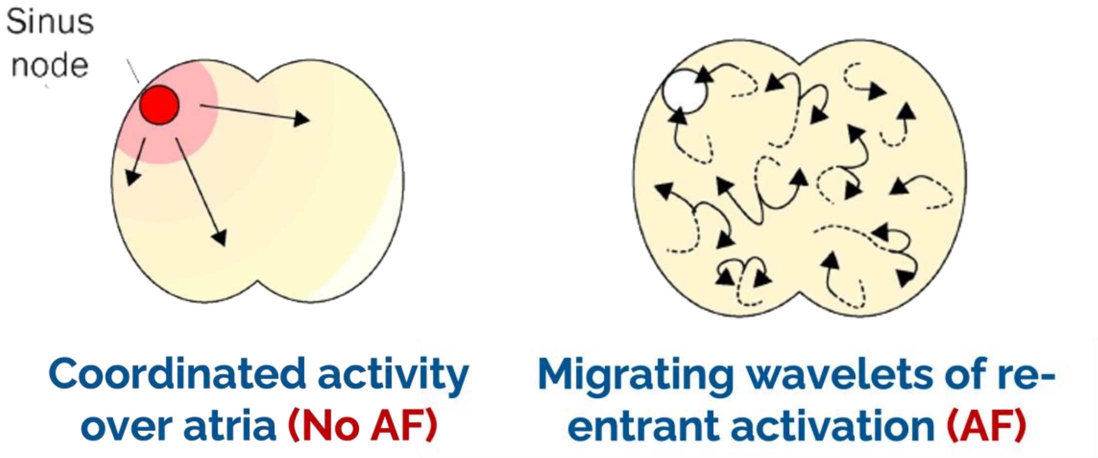




Motivation for Atrial Fibrillation Modelling

Atrial Fibrillation

- Most prevalent sustained arrhythmia in US & UK
- AF leads to diminished quality of life, heart failure, morbidity
- AF associated with increased risk of stroke



Narayan, S. M. et al.. Atrial fibrillation. *The Lancet*, 1997.

Long-term success rate from persistent AF reaches ~21% after conventional methods of treatment.

Brooks et al., Outcomes of long-standing persistent atrial fibrillation ablation: a systematic review, Heart Rhythm, 2015.

Motivation for Atrial Fibrillation Modelling

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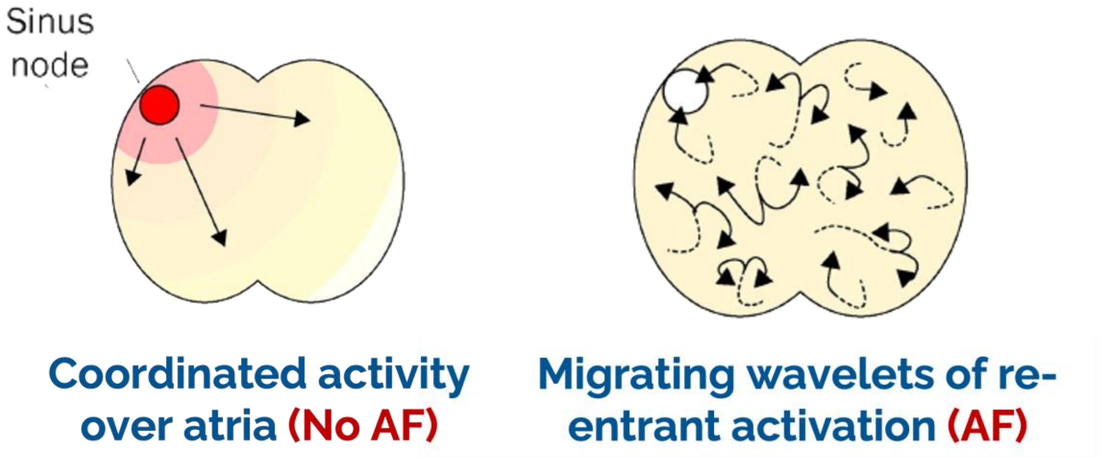
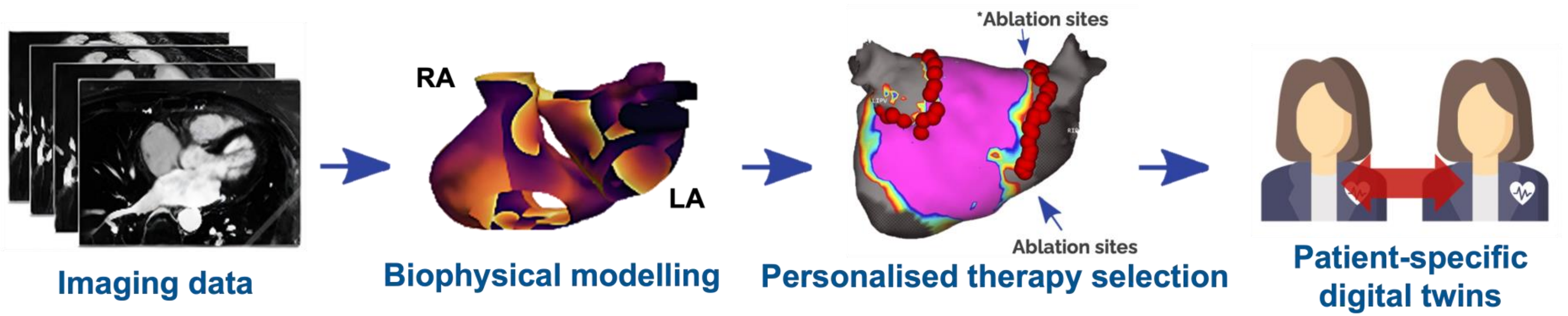


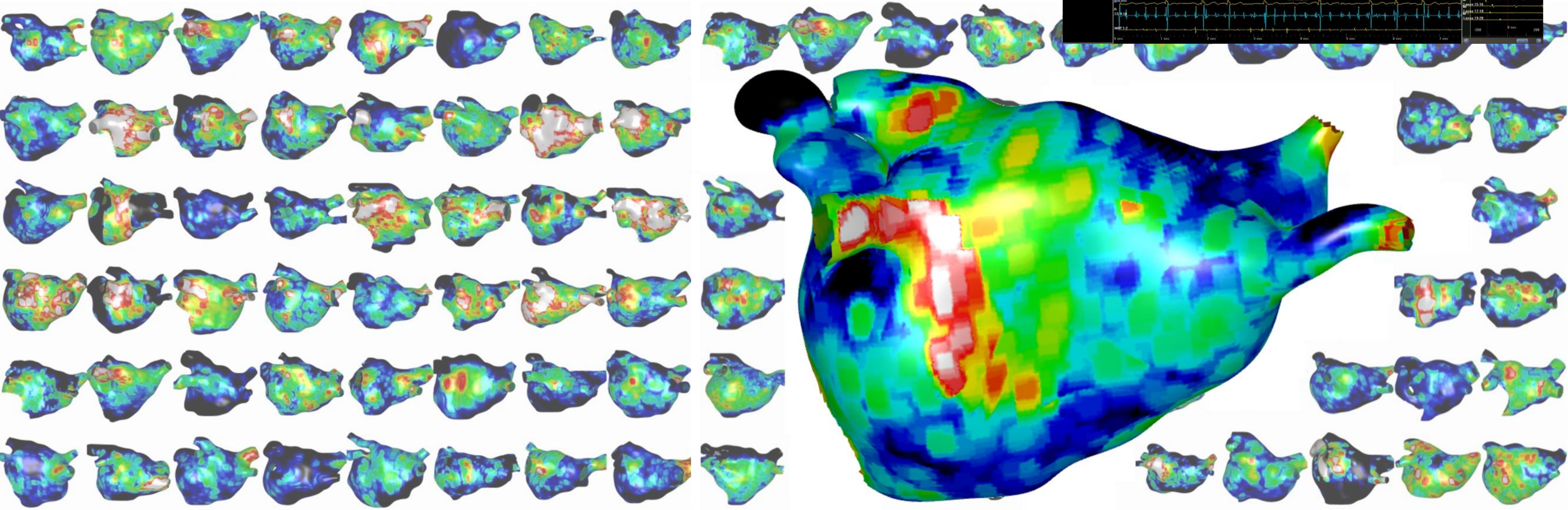
Narayan, S. M. et al.. Atrial fibrillation. *The Lancet*, 1997.

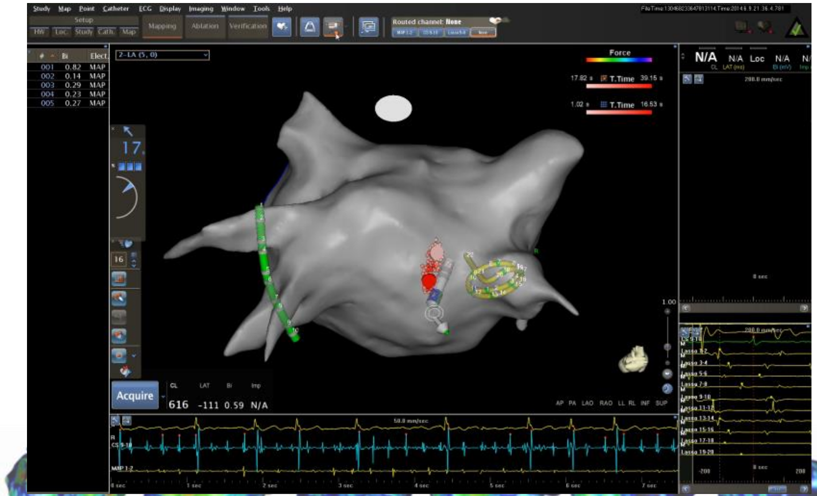


R. Karim et al, Acutus medical initiates ce mark study for focal pulsed field ablation therapy to treat atrial fibrillation. (2020)

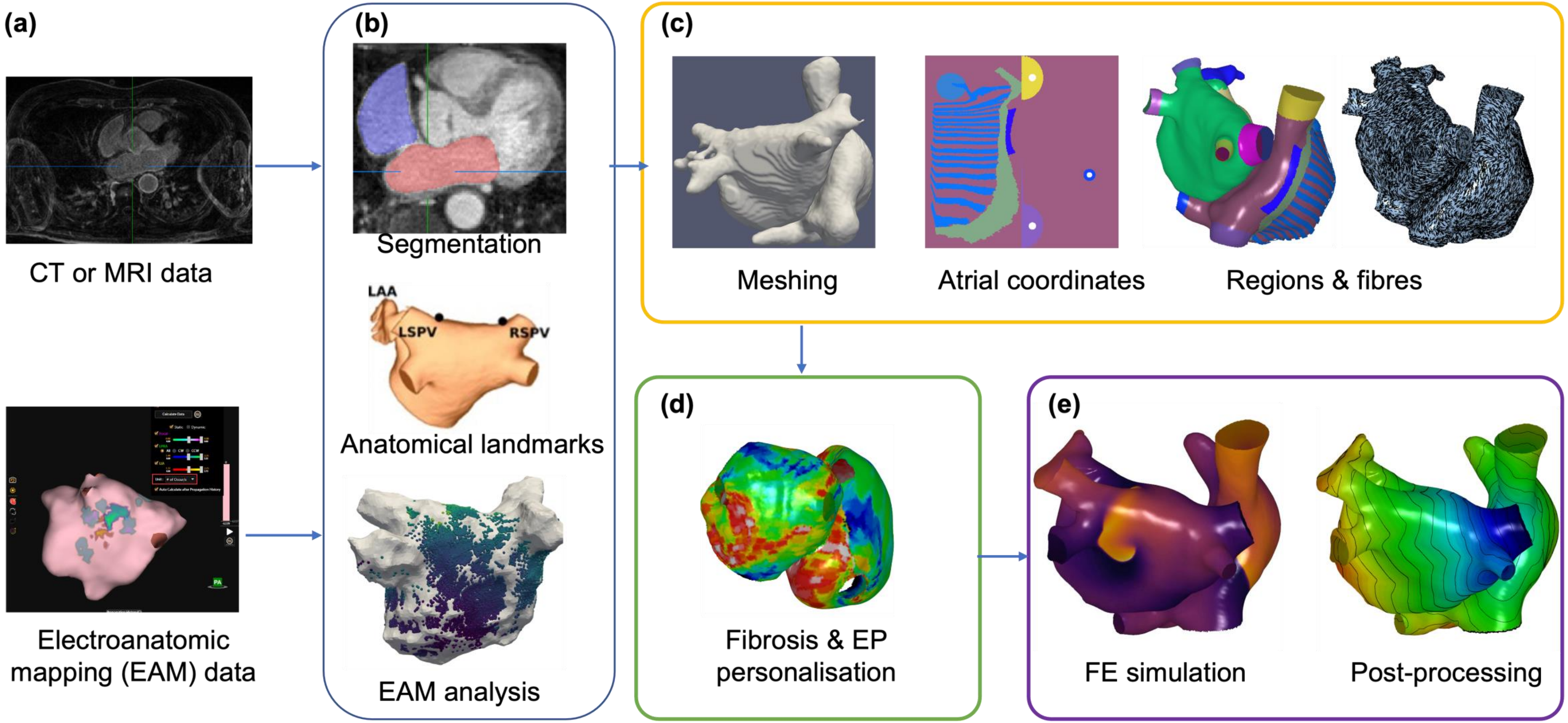
Personalised Computational Medicine

- Data explosion
- Virtual trials
- Personalised treatments?





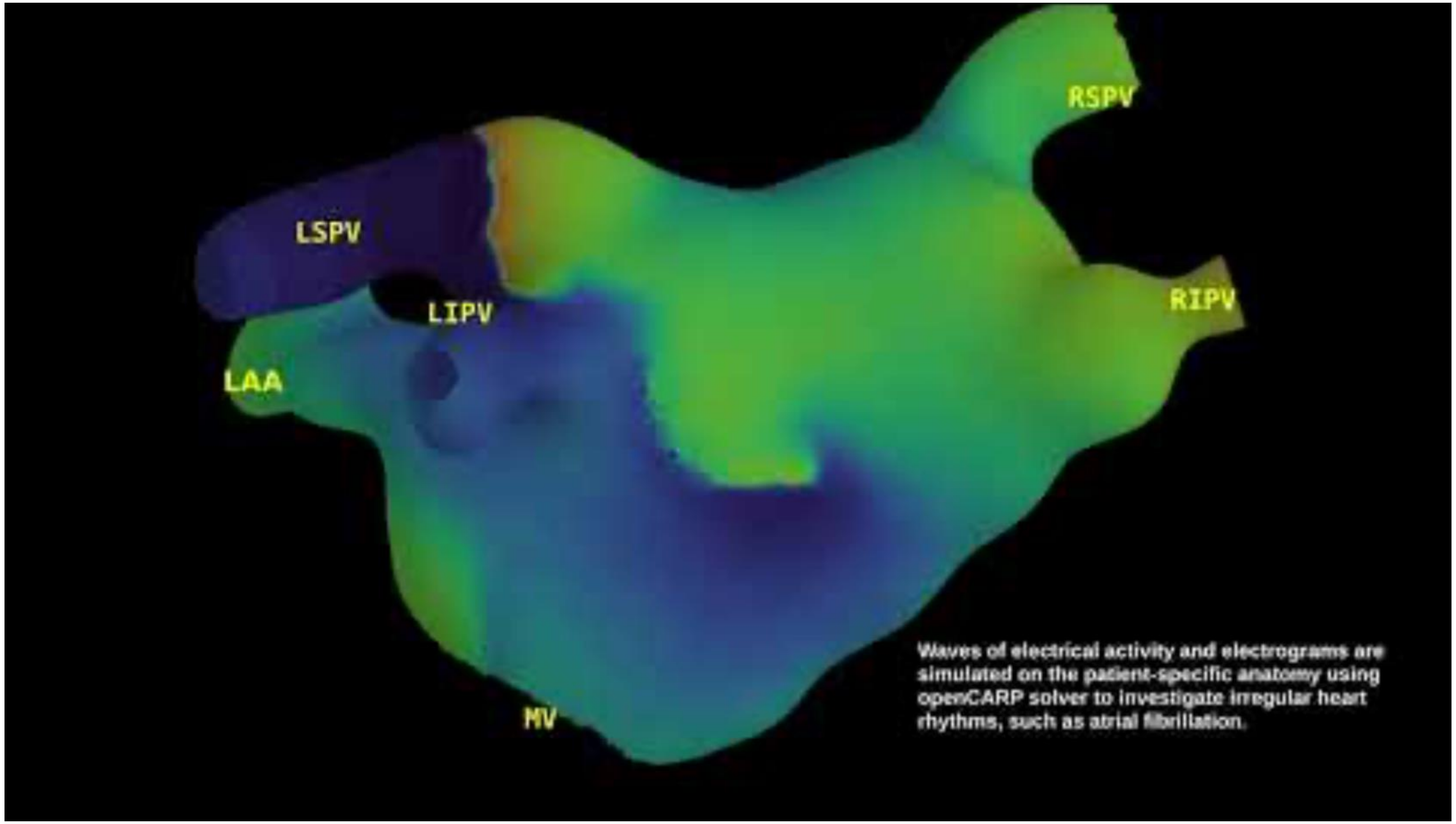
Model Pipeline



Roney, C.H. *et al.* (2023), Constructing bilayer and volumetric atrial models at scale. *Interface focus*, *13*(6), p.20230038.

Model Pipeline

In silico model for assessing individual responses to irregular heart rhythm treatments



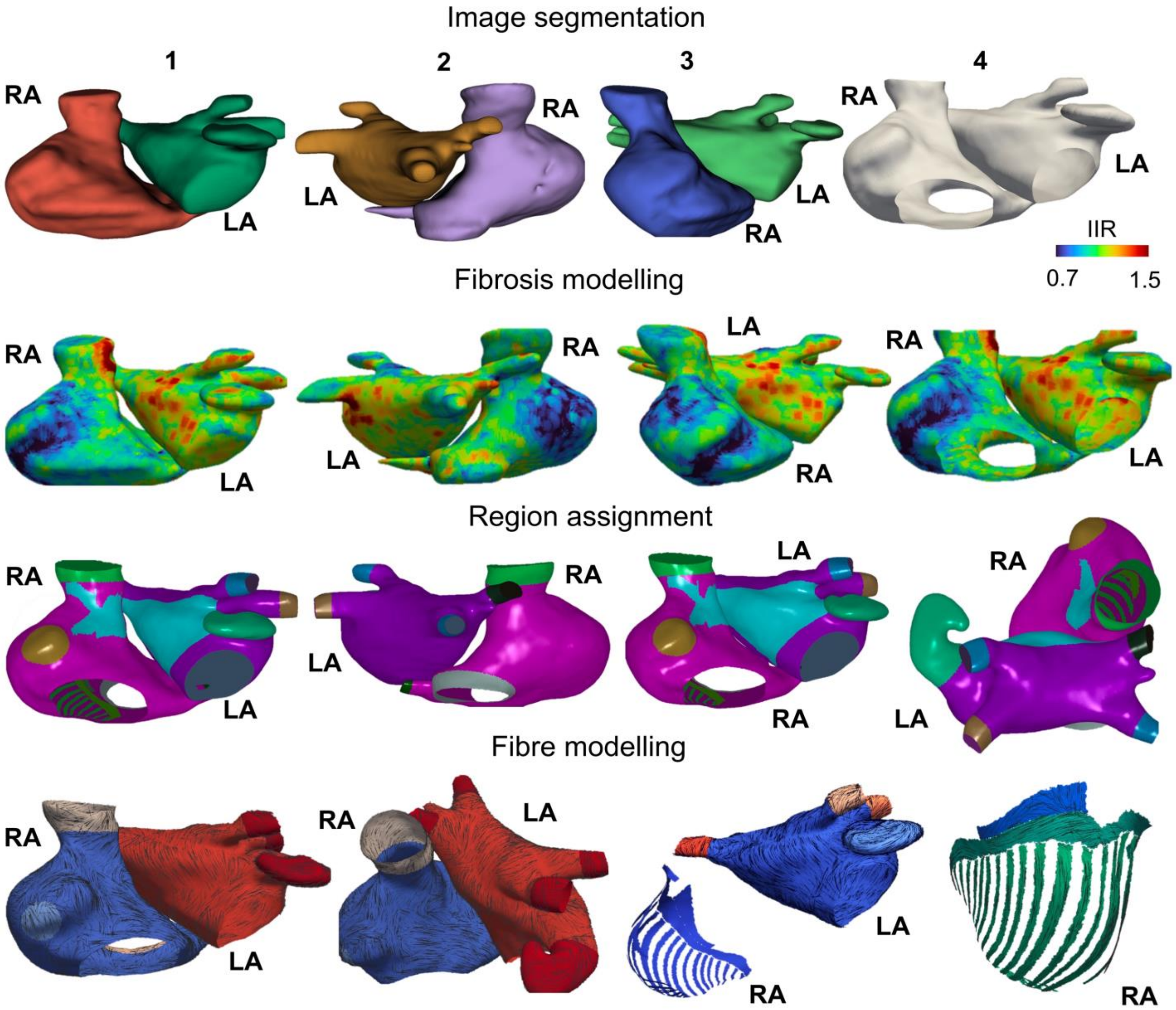
Carlos Edgar Lopez Barrera, Winning Early Career entry Archer2 Image and Video Competition 2023

Modelling for Atrial Fibrillation

Applications of cardiovascular use case

- Mechanistic investigation: change e.g. fibres, fibrosis, etc. in patient-specific models
- Investigate effects on electrophysiology, fibrillatory dynamics & treatment outcomes
- Developing optimal patient-specific treatments
- Large in silico trials
- Machine learning for longer term predictions on clinical timescales

Model generation:

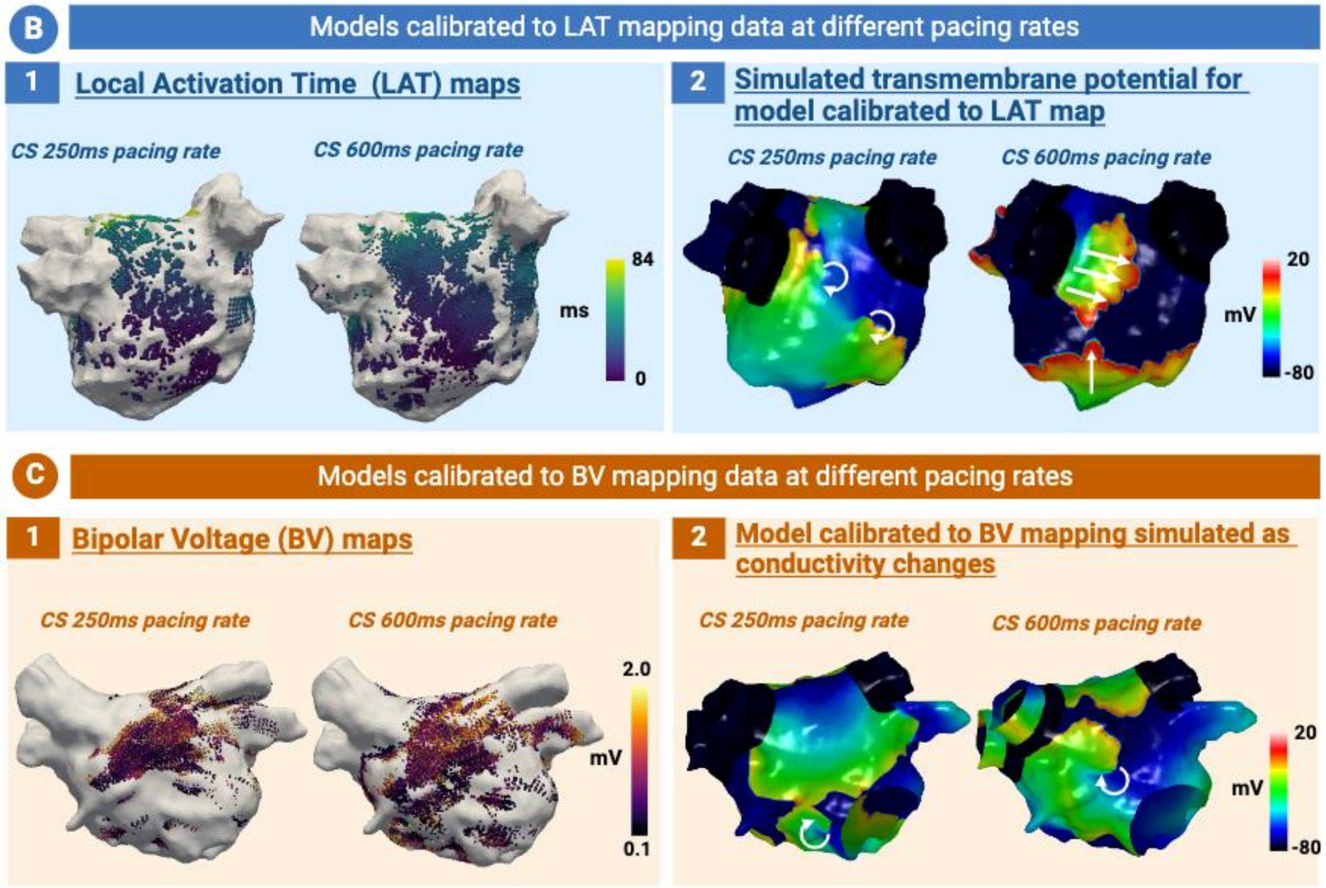


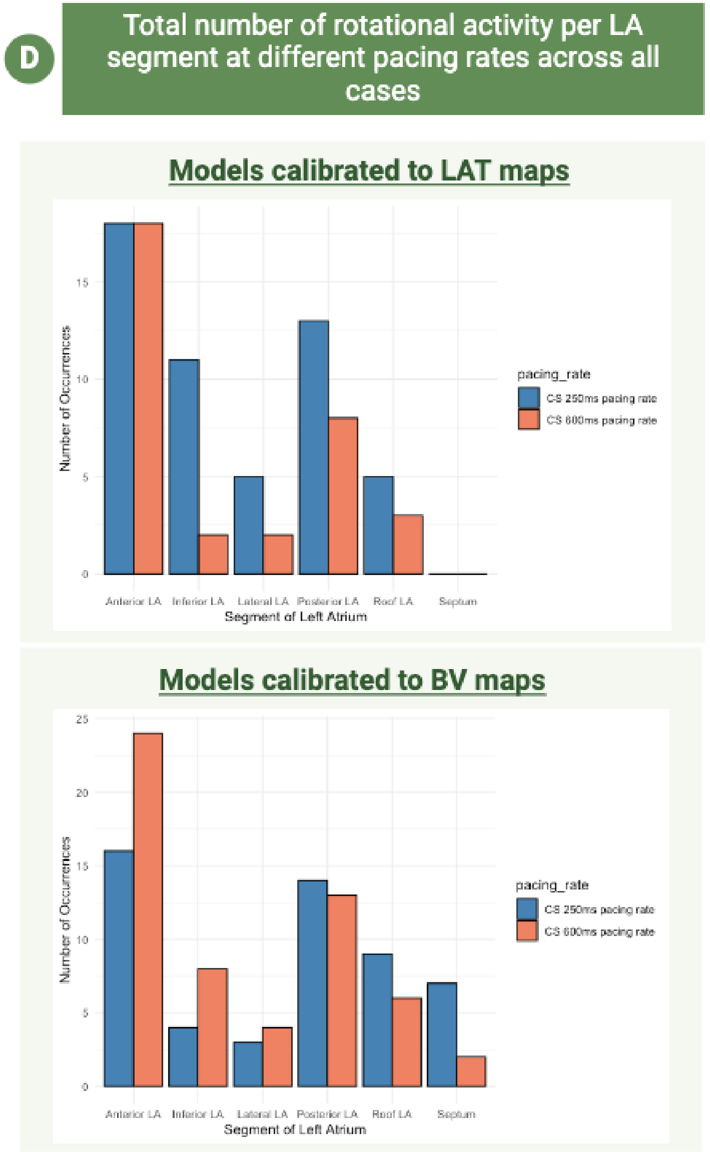
Pipeline:

Semhar Misghina: "Biatrial Modelling for In Silico Prediction of Atrial Fibrillation Inducibility", CinC 2023

Roney C et al. Constructing a Human Atrial Fibre Atlas. Ann Biomed Eng. 2020.

Calibrating electrical properties:

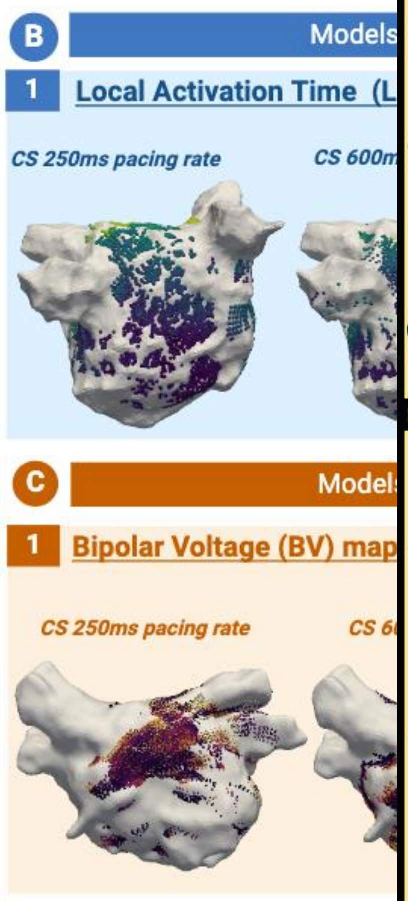


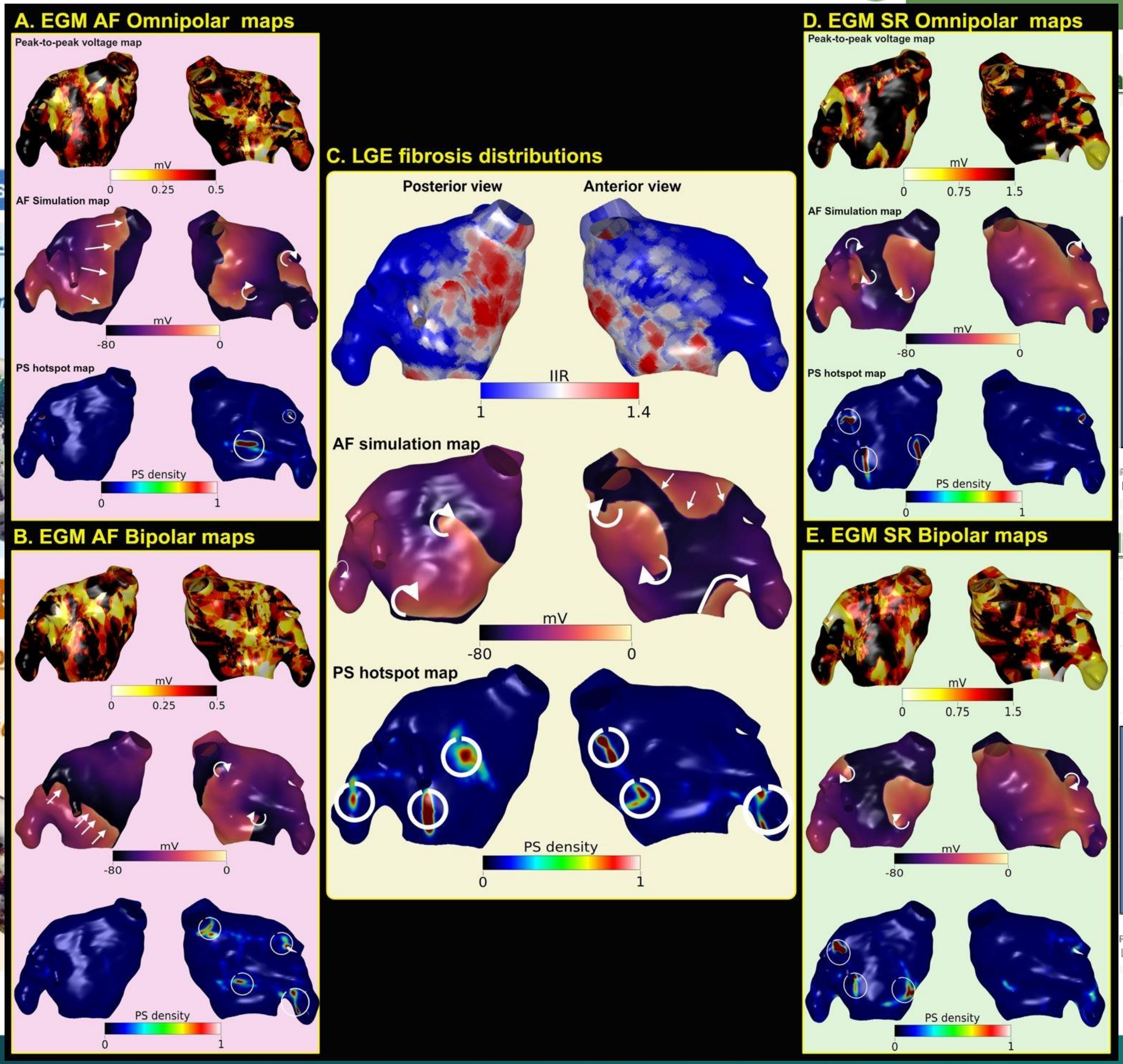


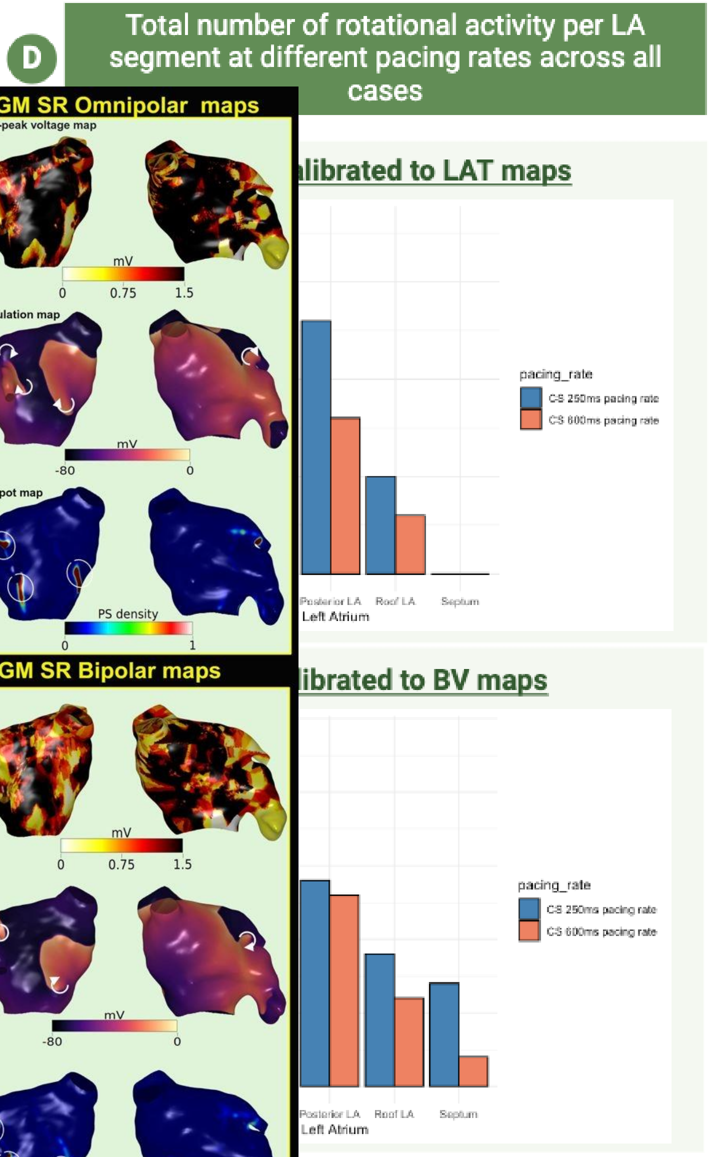
Caterina Vidal Horrach

Caterina Vidal Horrach & Dr Shohreh Honarbakhsh: “Patient-specific Atrial Fibrillation Simulation Prediction Depend on Rhythm Used for Calibration”, CinC 2023

Calibrating electrical properties:



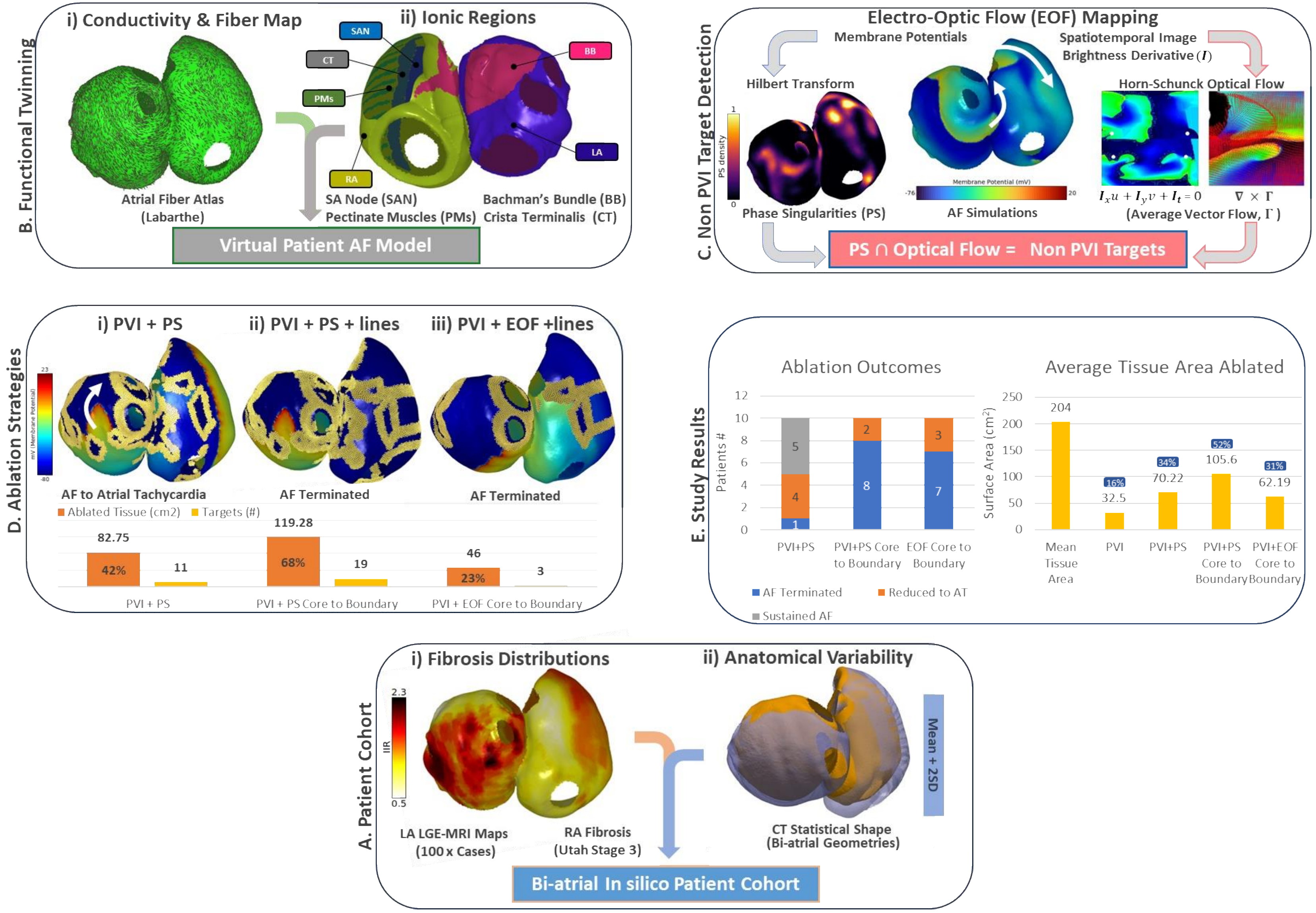




Caterina Vidal Horrach

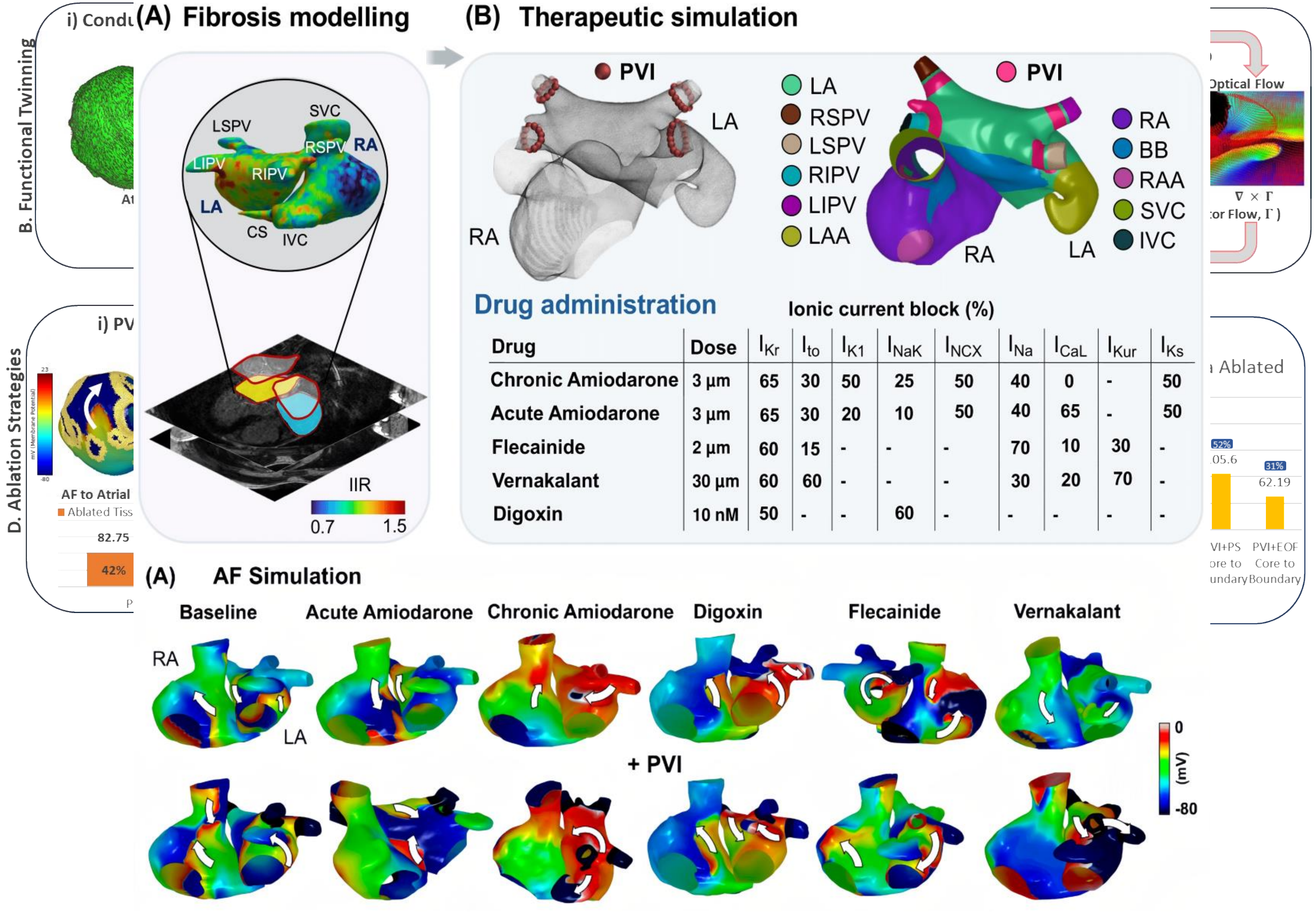
Dr Mahmoud Ehnesh

Ablation approaches and anti-arrhythmic drug therapies:



Ovais Jaffery

Ablation approaches and anti-arrhythmic drug therapies:



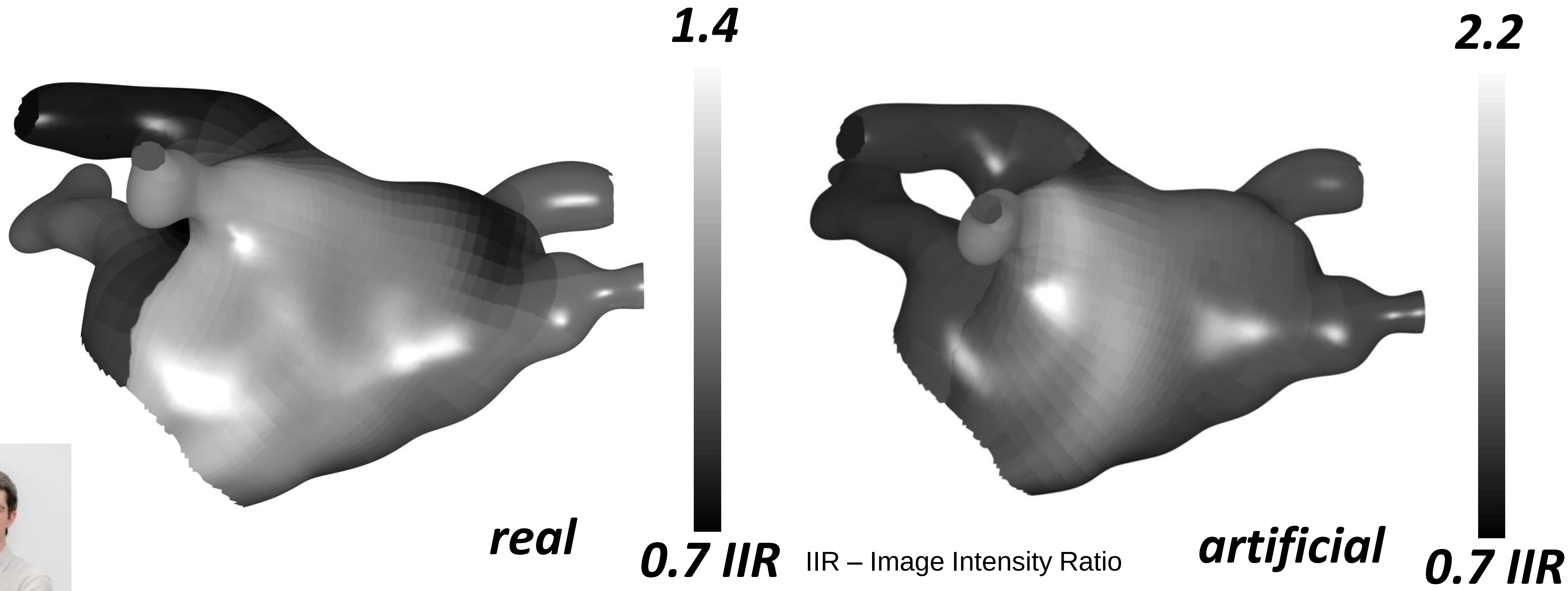
Drug	Dose	I_{Kr}	I_{to}	I_{K1}	I_{NaK}	I_{NCX}	I_{Na}	I_{CaL}	I_{Kur}	I_{Ks}
Chronic Amiodarone	3 μm	65	30	50	25	50	40	0	-	50
Acute Amiodarone	3 μm	65	30	20	10	50	40	65	-	50
Flecainide	2 μm	60	15	-	-	-	70	10	30	-
Vernakalant	30 μm	60	60	-	-	-	30	20	70	-
Digoxin	10 nM	50	-	-	60	-	-	-	-	-

Semhar Misghina

Ovais Jaffery

Large virtual cohort modelling:

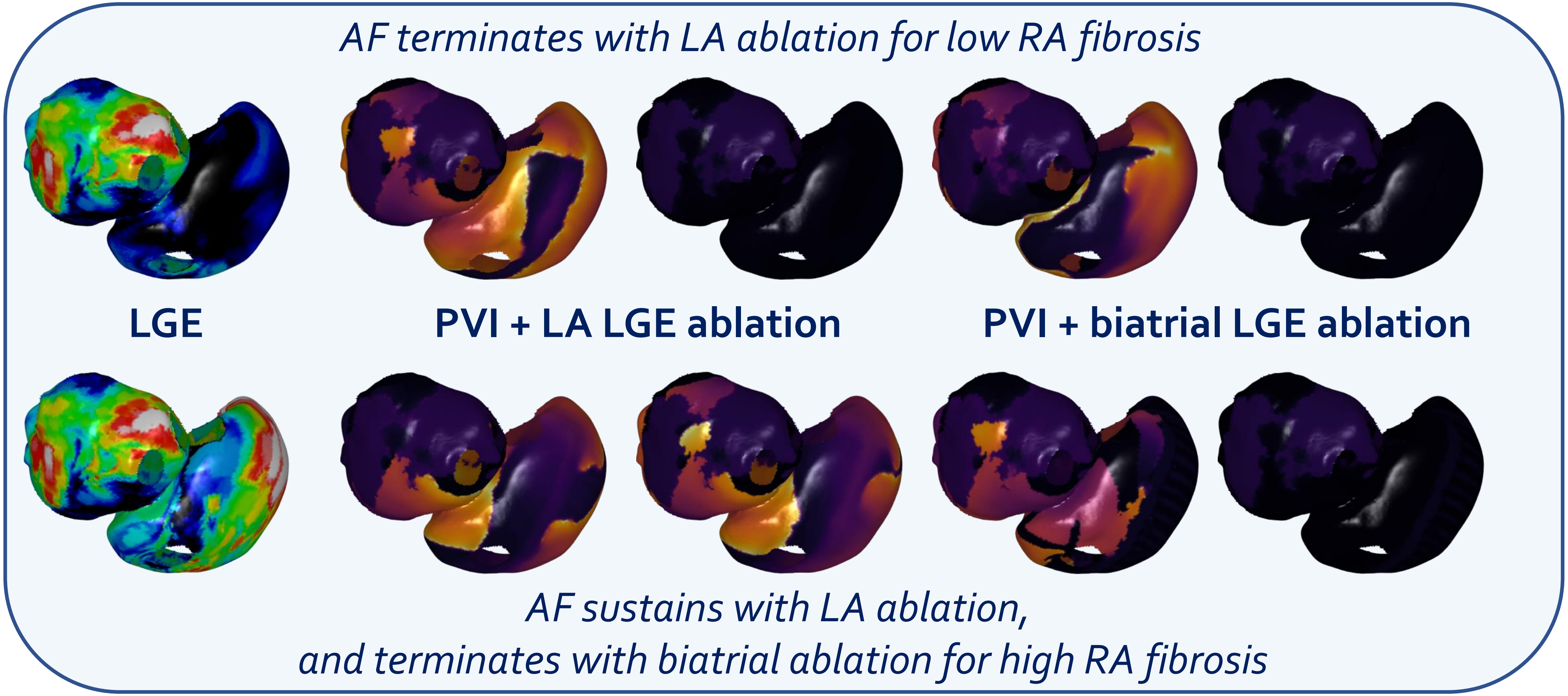
AF terminates with LA ablation for low RA fibrosis



Dr Alexander Zolotarev: "Atrial Fibrosis Distribution Generation based on the Diffusion Model", CinC 2023

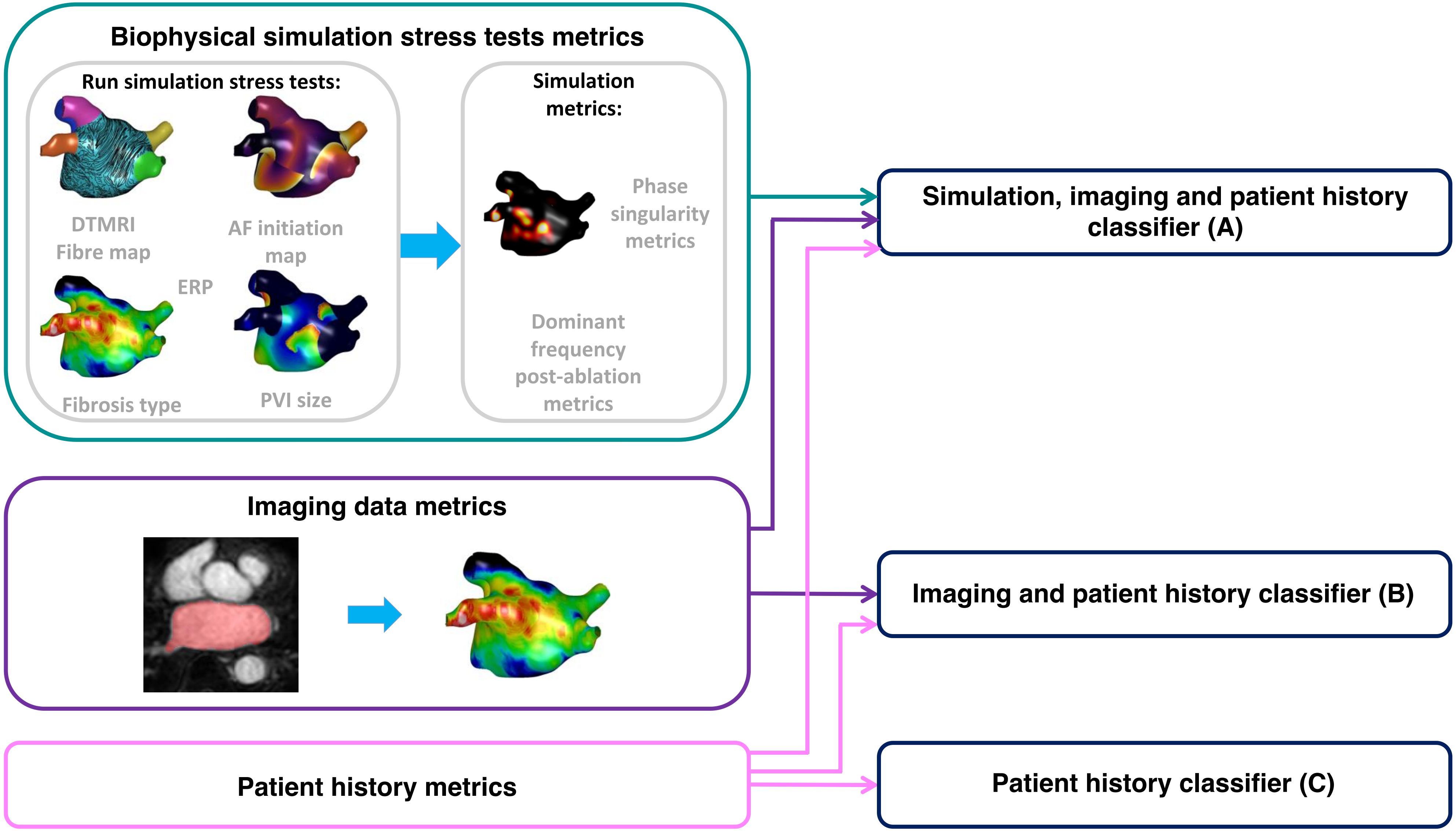
ɔo atrial

Large virtual cohort modelling:



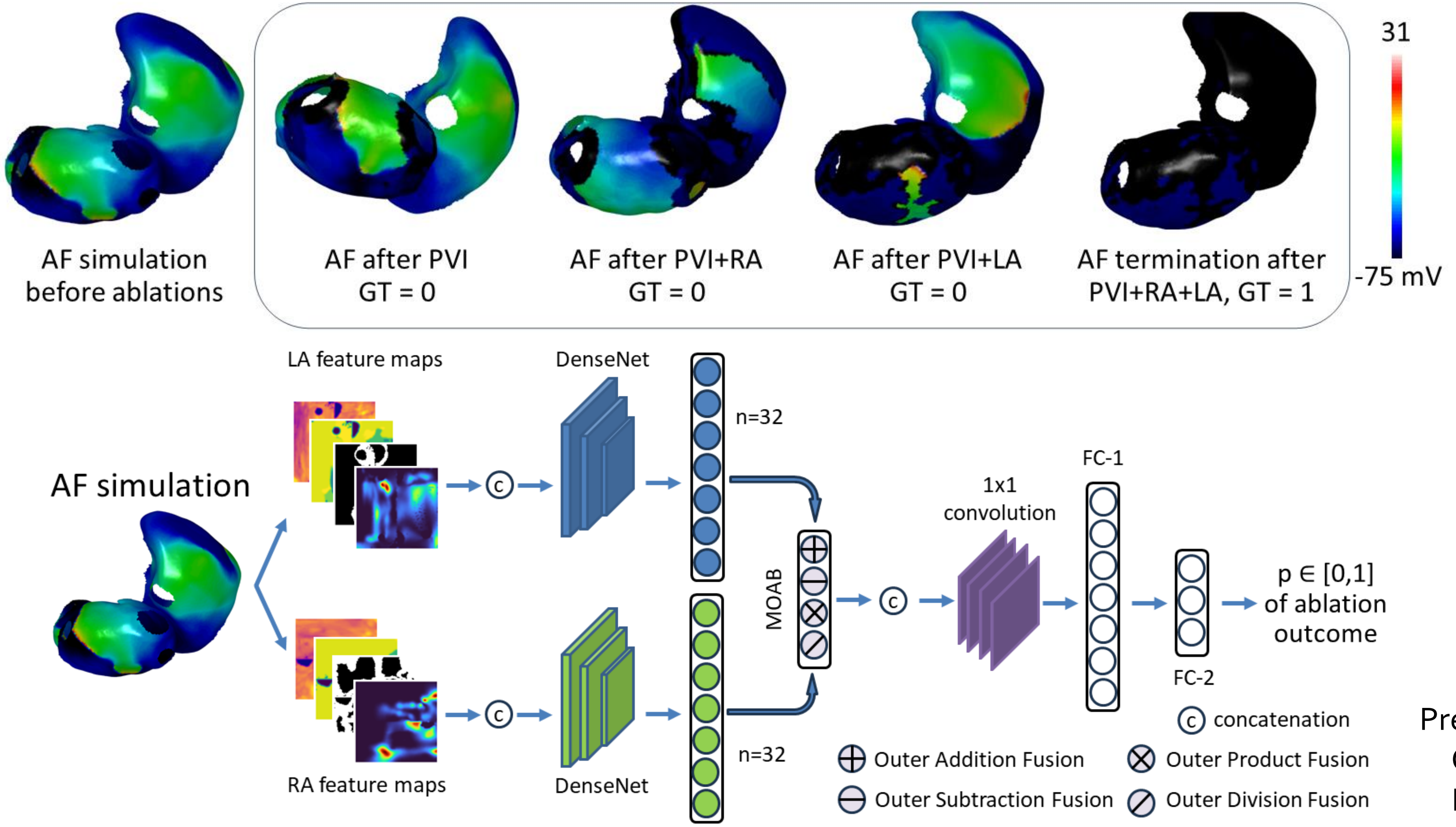
Comparing ablation approaches in a virtual cohort of 4000 patients, constructed using 4 fibrosis distributions applied to 1000 atrial anatomies from a statistical shape model

Combining patient-specific modelling and population data…:



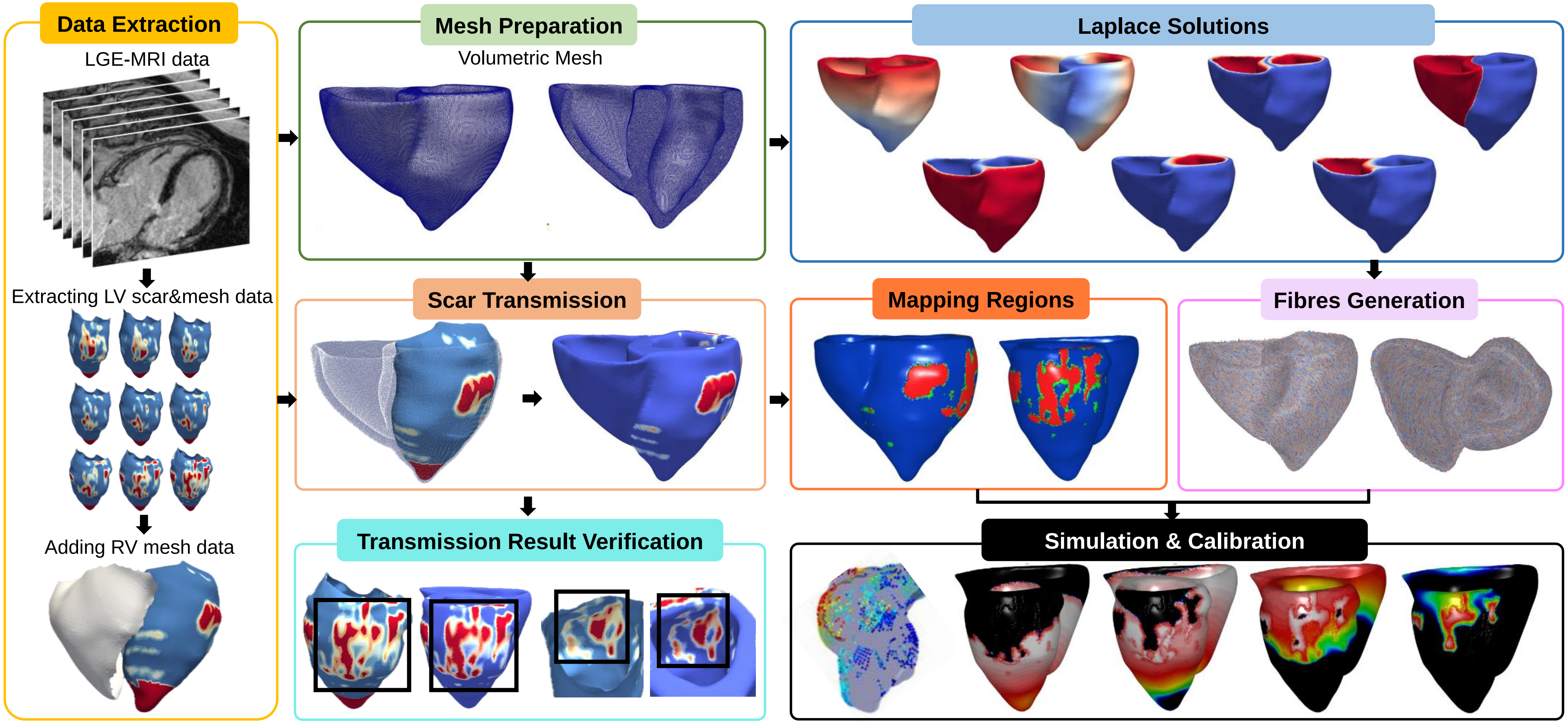
Roney CH et al. Predicting Atrial Fibrillation Recurrence by Combining Population Data and Virtual Cohorts of Patient-Specific Left Atrial Models. Circulation Arrhythmia & Electrophysiology (2022)

…and using deep learning to predict outcomes:



Dr Alexander Zolotarev
Predicting Atrial Fibrillation Treatment Outcome with Siamese Multi-modal Fusion and Digital Twins, MIDL 2024

In-silico ventricular tachycardia therapy:



Dr Fuyu Cheng

Coming soon: **ventricularmtk**

Cardiovascular use case: github pipeline

- Pipeline for constructing personalised models for atrial fibrillation (AF) to be integrated into proof-of-concept repository & platform for the VHT
- Source code, examples, instructions, computational & user requirements
- Open source: https://github.com/pcmlab/atrialmtk/

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Constructing bilayer and volumetric atrial models at scale

Caroline H. Roney, Jose Alonso Solis Lemus, Carlos Lopez Barrera, Alexander Zolotarev, Onur Ulgen, Eric Kerfoot, Laura Bevis, Semhar Misghina, Caterina Vidal Horrach, Ovais A. Jaffery, Mahmoud Ehnesh, ... See all authors

Published: 15 December 2023 | https://doi.org/10.1098/rsfs.2023.0038

Instructions for landmark selection

1. **Landmark selection for the left atrium**

General point selection

First, roughly select a point somewhere on each anatomical landmark that is listed in Rough_Point_Picking.py. If the pulmonary veins are close together, select points on opposite sides of each (i.e. as far from another vein as possible); the script uses these points to assign which vein is which. The LAA tip point is used as a boundary condition location of the Laplace-Dirichlet solve. Make sure to do this in the same order as in the script:

i) Right superior pulmonary vein (RSPV)

ii) Right inferior pulmonary vein (RIPV)

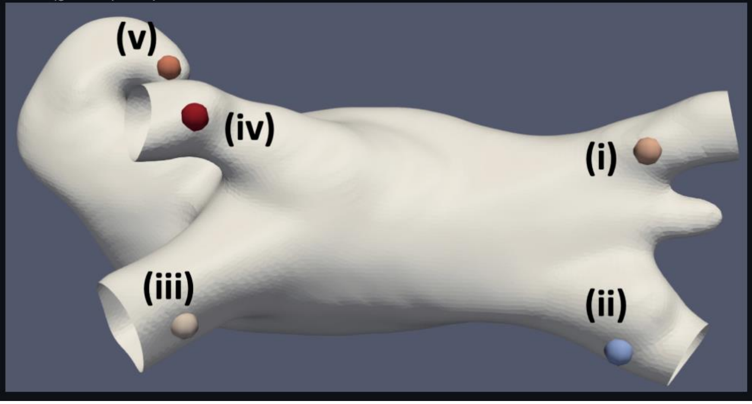
iii) Left inferior pulmonary vein (LIPV)

iv) Left superior pulmonary vein (LSPV)

v) Left atrial appendage tip (LAA tip)

vi) Left atrial appendage base (LAA base)

View 1 (general points):



Roney, C.H., *et al.* (2023), Constructing bilayer and volumetric atrial models at scale. *Interface focus*, *13*(6), p.20230038

Cardiovascular use case: workflows

Workflow 1:

This workflow takes a segmentation mask as input, which can be produced f
input directly by the user if already provided. The steps to run these exampl

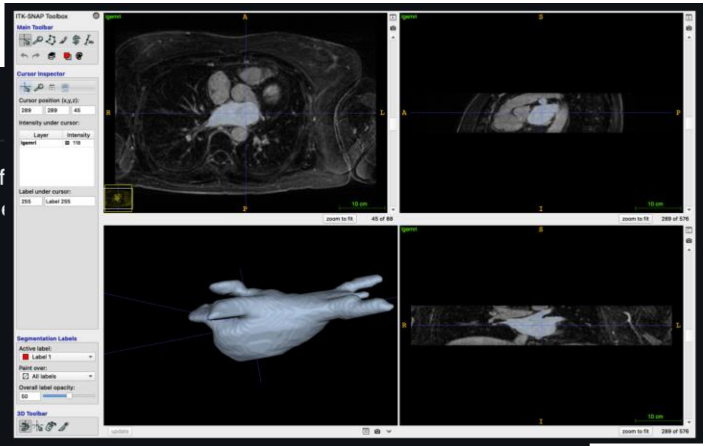
0ImagingData

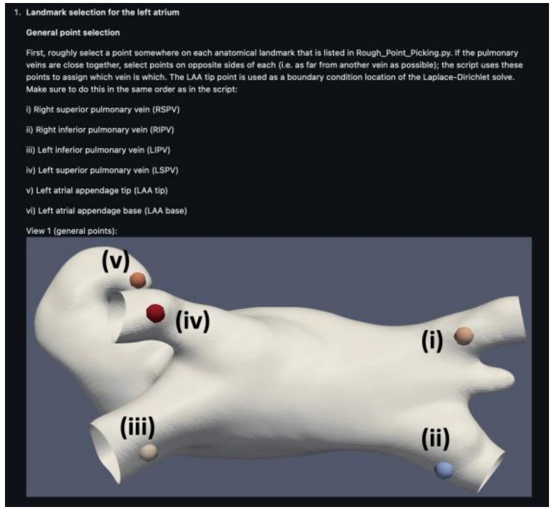
1Clipping

2Landmarks

3Processing

4Simulation





Workflow 2:

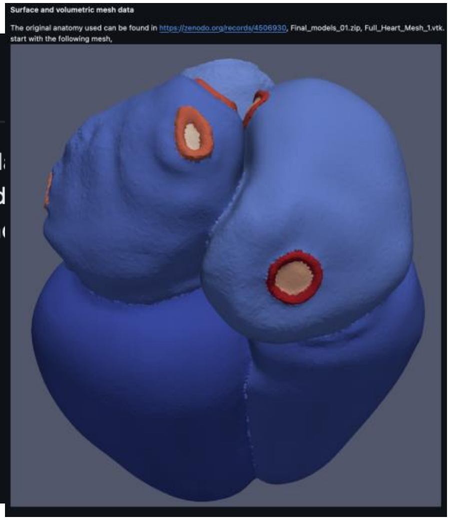
This workflow applies where the user is provided with the surface file rather than the imaging d
artificial datasets, for example, statistical shape model data. Since it starts from atrial surface d
vessels, it does not include the 0ImagingData or 1Clipping steps from workflow 1 and we Instea

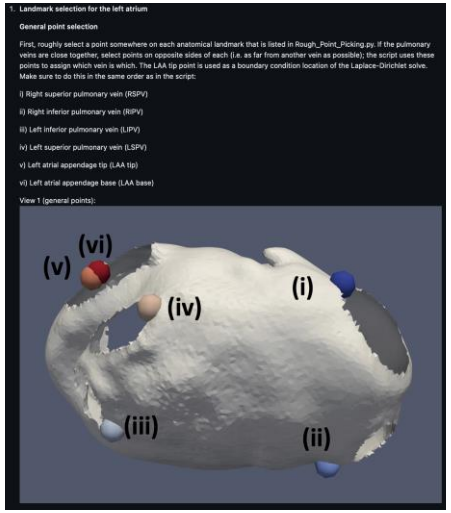
0SurfaceMeshData

2Landmarks

3Processing

4Simulation





Cardiovascular use case: workflows

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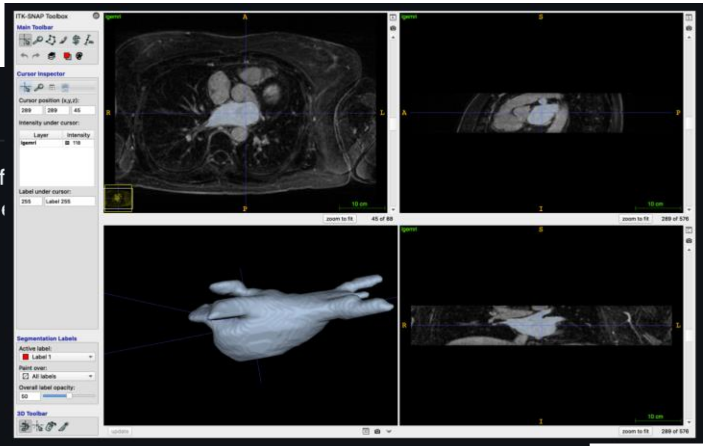
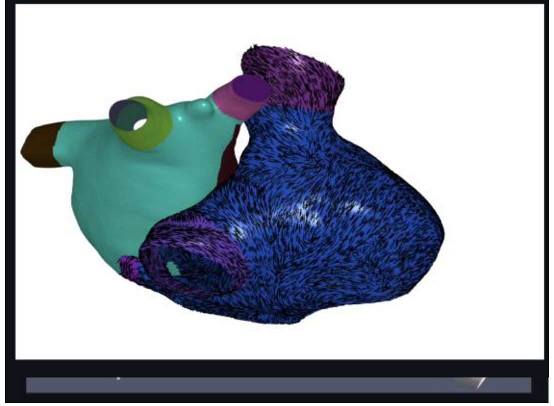


1. Landmark selection for the left atrium

General point selection

Example-Biatrial-MRI

This example generates a biatrial bilayer model from the Atrial Challenge dataset (see Dataset.txt). This example can be run after the Example-LeftAtrium to add the right atrial component and interatrial connections to produce the biatrial model. The steps are detailed in the same categories as for Example-LeftAtrium.



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0SurfaceMeshData

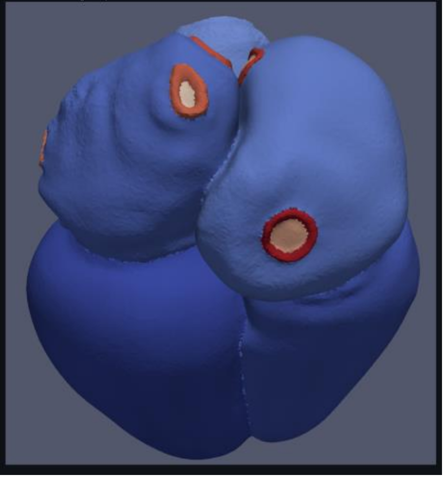
2Landmarks

3Processing

4Simulation

Surface and volumetric mesh data

The original anatomy used can be found in https://zenodo.org/records/4506930, Final_models_01.zip, Full_Heart_Mesh_1.vtk. start with the following mesh,

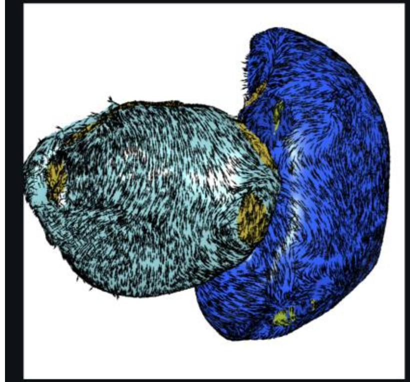


1. Landmark selection for the left atrium

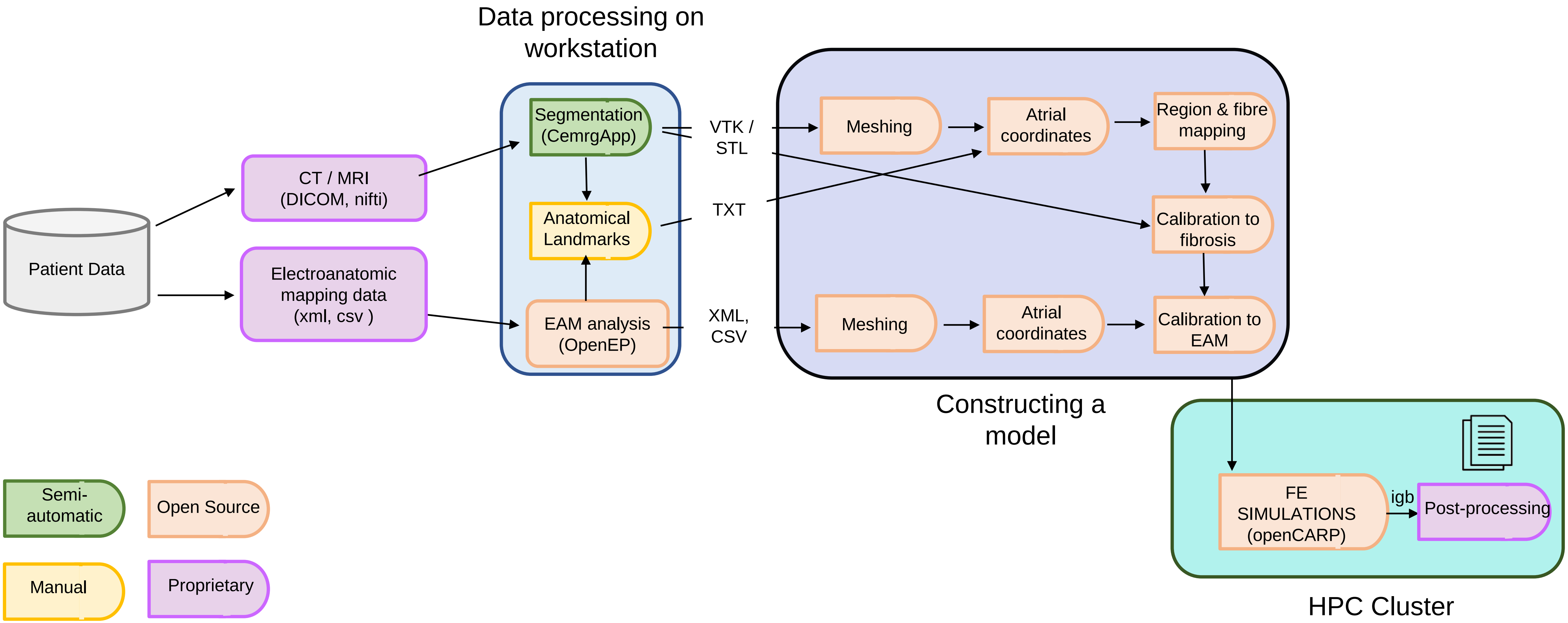
General point selection

Example-Biatrial-CT-shape-model

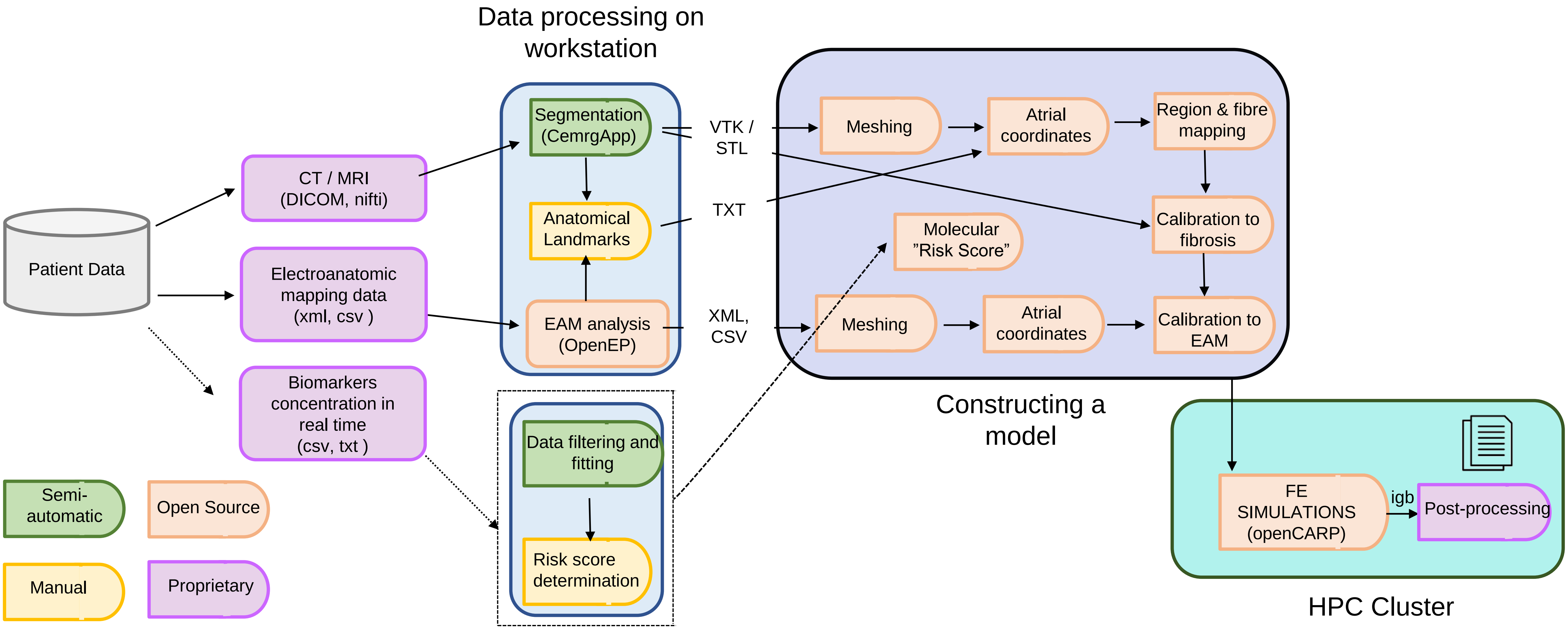
This example generates biatrial models from a statistical shape model of the atria derived using CT scans of a healthy adult population (see Dataset.txt). We start with the atrial surfaces and progress through the above steps to generate two versions of the model: one in bilayer format (triangular mesh) and the other in volumetric format (tetrahedral mesh).



Cardiovascular use case: data flow



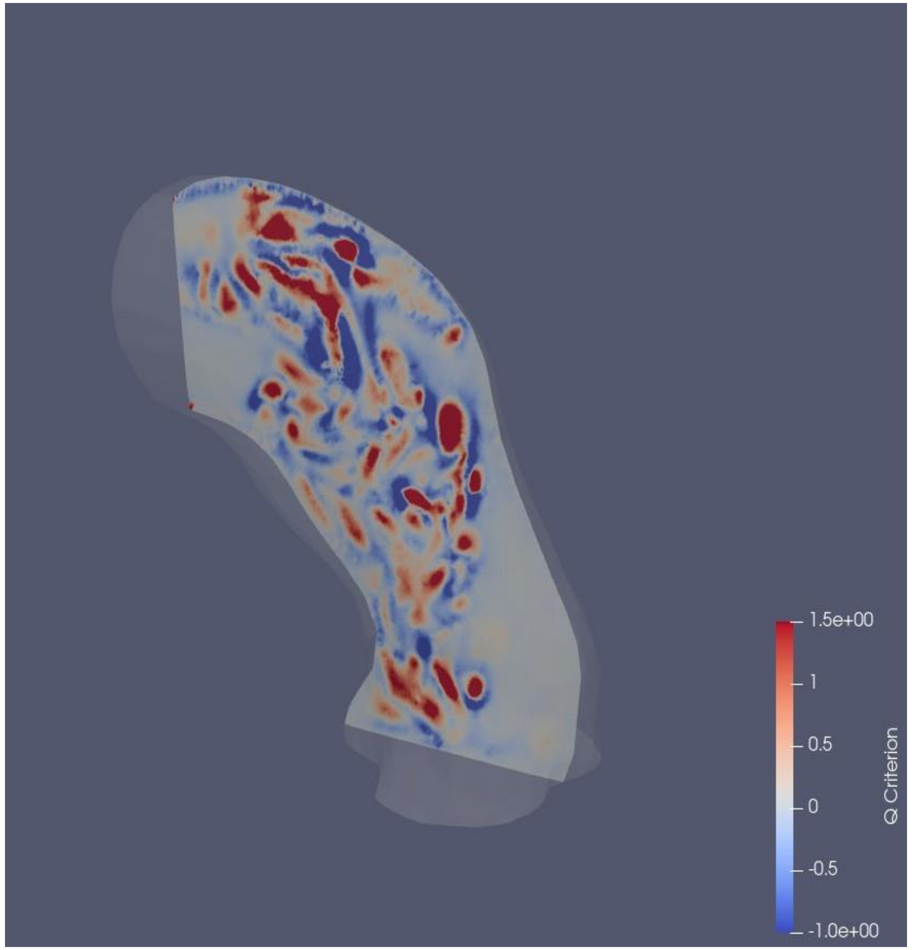
Cardiovascular use case: data flow



Cardiovascular use case

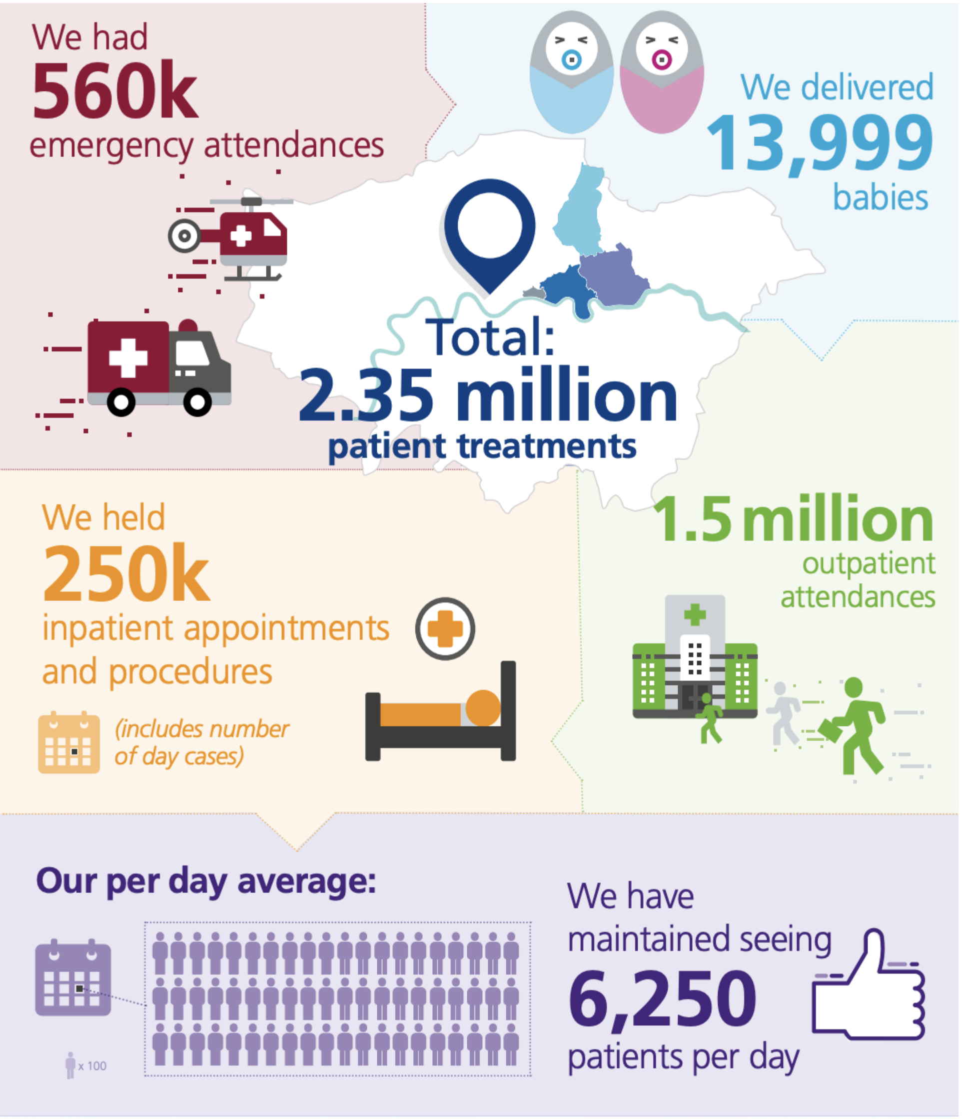
Integration in VHT systems

- Integrating different biophysical models: electrophysiology, mechanics, fluids
- Integrating across spatial scales: from cellular changes to organ level changes
- Multi-organ: brain – heart interactions
- Infrastructure requirements



Integration in VHT systems in the clinic

NHS
Barts Health
NHS Trust



Delivering care across North-East London

- Turnover - approx. £2bn
- Capital programmes - approx. £60m/year
- Workforce - 24k people

Interested??

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Research

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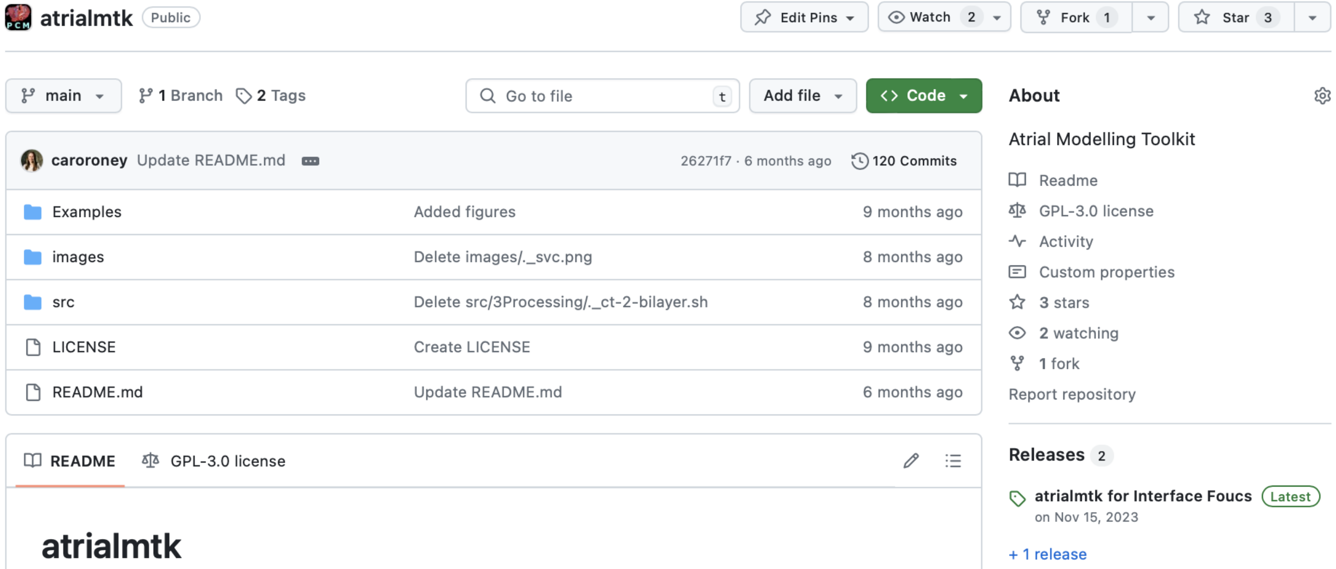
Cite this article: Roney CH *et al.* 2023 Constructing bilayer and volumetric atrial models at scale. *Interface Focus* **13**: 20230038.

Constructing bilayer and volumetric atrial models at scale

Caroline H. Roney[1,2], Jose Alonso Solis Lemus[2,3], Carlos Lopez Barrera[1,4], Alexander Zolotarev[1], Onur Ulgen[2], Eric Kerfoot[2], Laura Bevis[1], Semhar Misghina[1], Caterina Vidal Horrach[1], Ovais A. Jaffery[1], Mahmoud Ehnesh[1], Cristobal Rodero[2,3], Dhani Dharmaprani[5], Gonzalo R. Ríos-Muñoz[6,7,8], Anand Ganesan[5], Wilson W. Good[9], Aurel Neic[10], Gernot Plank[11,12], Luuk H. G. A. Hopman[13], Marco J. W. Götte[13], Shohreh Honarbakhsh[14], Sanjiv M. Narayan[15], Edward Vigmond[16,17] and Steven Niederer[2,3,18]



Cardiovascular use case: 100 open-source patient-specific models

open CARP

Cardiovascular

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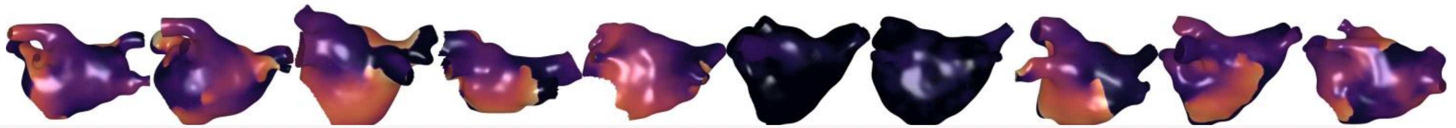

https://zenodo.org/record/5801337

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January 31, 2022 | Dataset | Open Access

Predicting atrial fibrillation recurrence by combining population data and virtual cohorts of patient-specific left atrial models

Roney, Caroline; Sim, Iain; Yu, Jin; Beach, Marianne; Mehta, Arihant; Solis-Lemus, Jose; Kotadia, Irum; Whitaker, John; Corrado, Cesare; Razeghi, Orod; Vigmond, Edward; Narayan, Sanjiv; O'Neill, Mark; Williams, Steven; Niederer, Steven

Abstract

Background: Current ablation therapy for atrial fibrillation is sub-optimal and long-term response is challenging to predict. Clinical trials identify bedside properties that provide only modest prediction of long-term response in populations, while patient-specific models in small cohorts primarily explain acute response to ablation. We aimed to predict long-term atrial fibrillation recurrence after ablation in large cohorts, by using machine learning to complement biophysical simulations by encoding more inter-individual variability.

Methods: Patient-specific models were constructed for 100 atrial fibrillation patients (43 paroxysmal, 41 persistent, 16 long-standing persistent), undergoing first ablation. Patients were followed for 1-year using ambulatory ECG monitoring. Each patient-specific biophysical model combined differing fibrosis patterns, fibre orientation maps, electrical properties and ablation patterns to capture uncertainty in atrial properties and to test the ability of the tissue to sustain fibrillation. These simulation stress tests of different model variants were post-processed to calculate atrial fibrillation simulation metrics. Machine learning classifiers were trained to predict atrial fibrillation recurrence using features from the patient history, imaging and atrial fibrillation simulation metrics.

Results: We performed 1100 atrial fibrillation ablation simulations across 100 patient-specific models. Models based on simulation stress tests alone showed a maximum accuracy of 0.63 for predicting long-term fibrillation recurrence. Classifiers trained to history, imaging and simulation stress tests (average ten-fold cross-validation area under the curve 0.85 ± 0.09, recall 0.80 ± 0.13, precision 0.74 ± 0.13) outperformed those trained to history and imaging (area under the curve 0.66 ± 0.17), or history alone (area under the curve 0.61 ± 0.14).

Conclusion: A novel computational pipeline accurately predicted long-term atrial fibrillation recurrence in individual patients by combining outcome data with patient-specific acute simulation response. This technique could help to personalise selection for atrial fibrillation ablation.

Dataset Description: We include surface meshes in vtk format, consisting of the nodes, triangular elements, the atrial

Publication date: January 31, 2022

DOI: DOI 10.5281/zenodo.5801337

Grants:

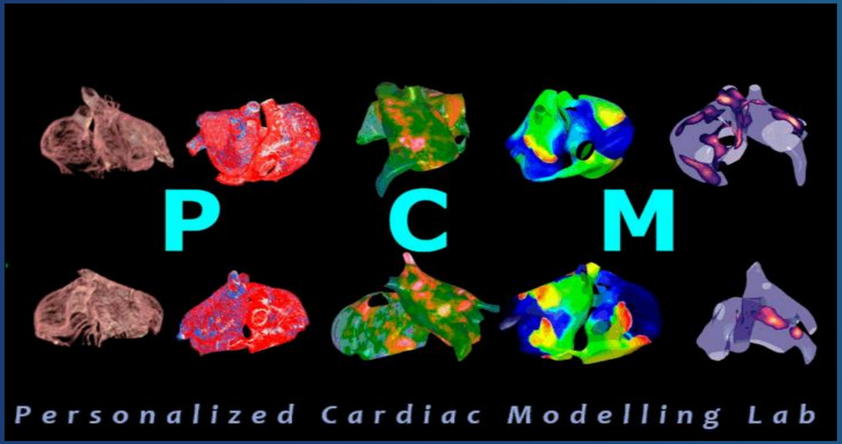
Research Councils UK:

- Predicting Atrial Fibrillation Mechanisms Through Deep Learning (MR/S015086/1)
- Personalised Model Based Optimal Lead Guidance in Cardiac Resynchronisation Therapy (EP/M012492/1)
- Wellcome EPSRC Centre for Medical Engineering (NS/A000049/1)
- Uncertainty Quantification in Prospective and Predictive Patient Specific Cardiac Models (EP/P01268X/1)

Queen Mary
University of London

Thank you

Dr Laura Bevis: l.bevis@qmul.ac.uk
PCM Lab: https://pcmlab.co.uk/contact-us/



Acknowledgements

Caterina Vidal Horrach
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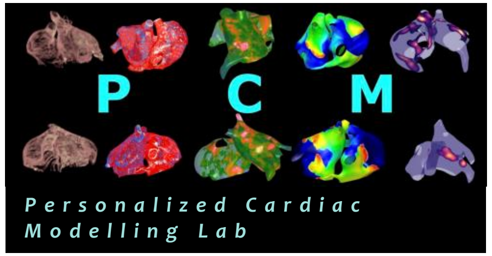

Queen Mary University of London — Digital Environment Research Institute

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UKRI Future Leaders Fellowships

NIHR | Barts Biomedical Research Centre

NHS Barts Health NHS Trust

Queen Mary University of London

Video showing steps for generating atrial models,
Archer2 image competition winner, Carlos Lopez Barrera

Acknowledgements

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Sam Coveney
Richard Clayton
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Steve Niederer
Cristobal Rodero
Fu Siong Ng
Nicholas Peters

Graz
Gernot Plank
Matthias Gsell
Karli Gillette
Aurel Neic

Stanford
Sanjiv Narayan
AJ Rogers

Liryc
Edward Vigmond
Jason Bayer
Hubert Cochet
Pierre Jais
Marianna Meo
Remi Dubois
Yingjing Feng

Queen Mary University of London

OpenEP

openCARP

Organ-on-a-Chip Technologies Network

carp cardiac arrhythmia research package

ACUTUS MEDICAL

KING'S College LONDON

MRC Medical Research Council

Researchers

Sofia Karvounari, Konstantinos Triantos , ATHENA research center

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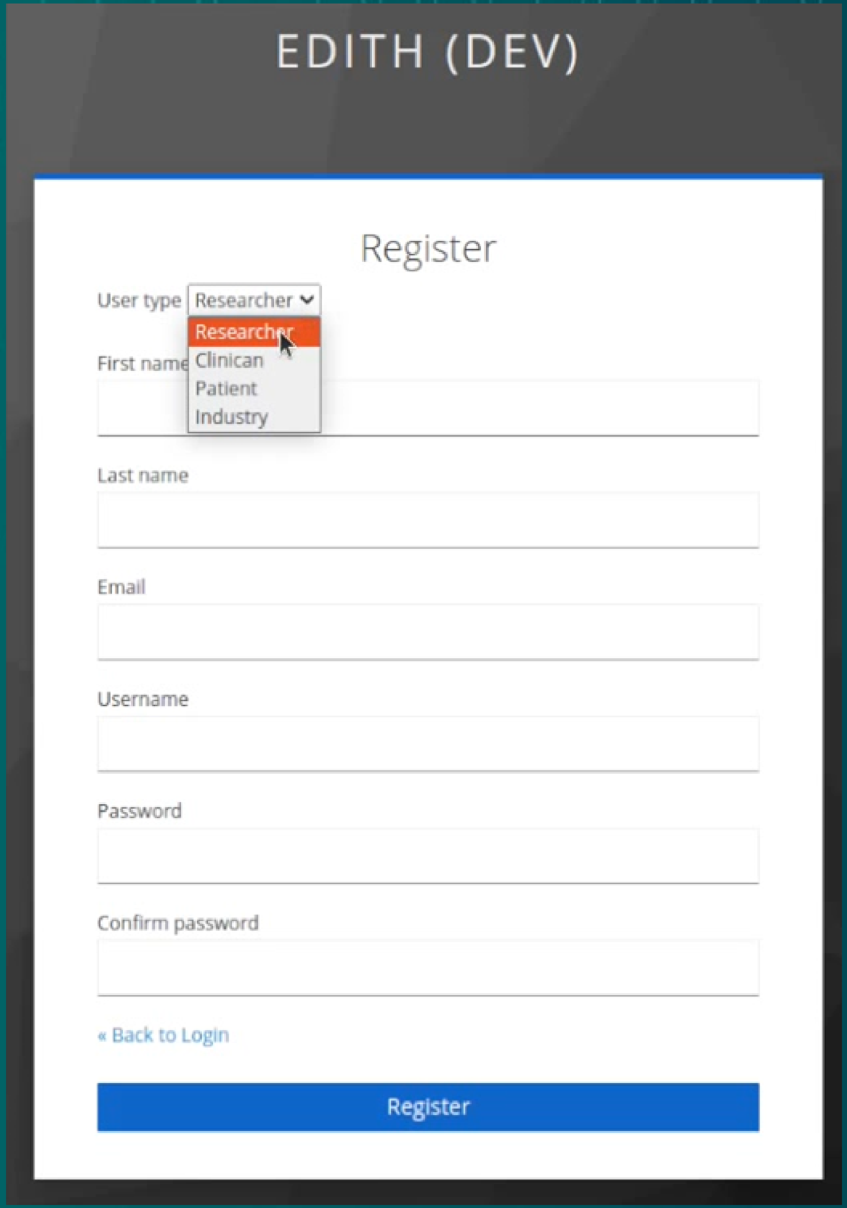
Researchers



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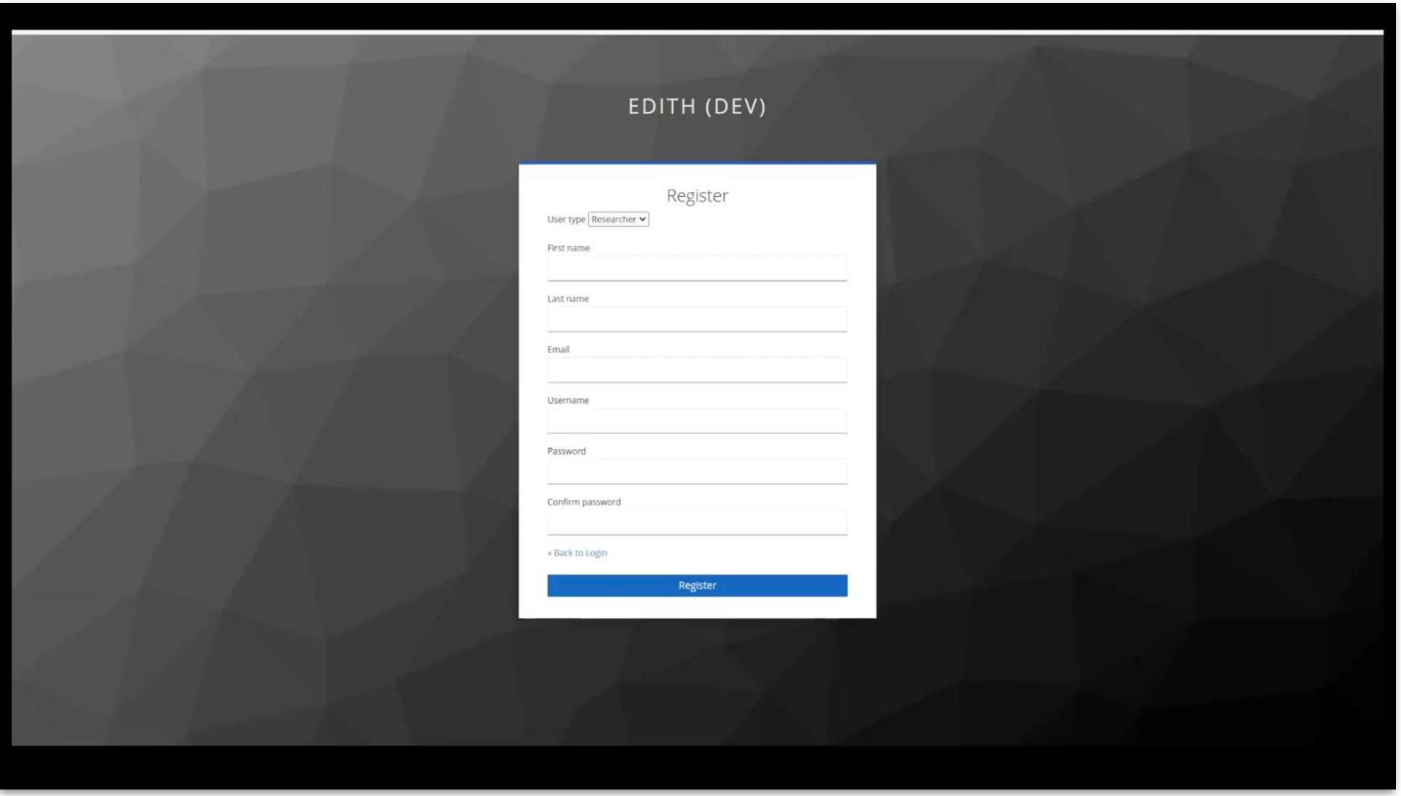
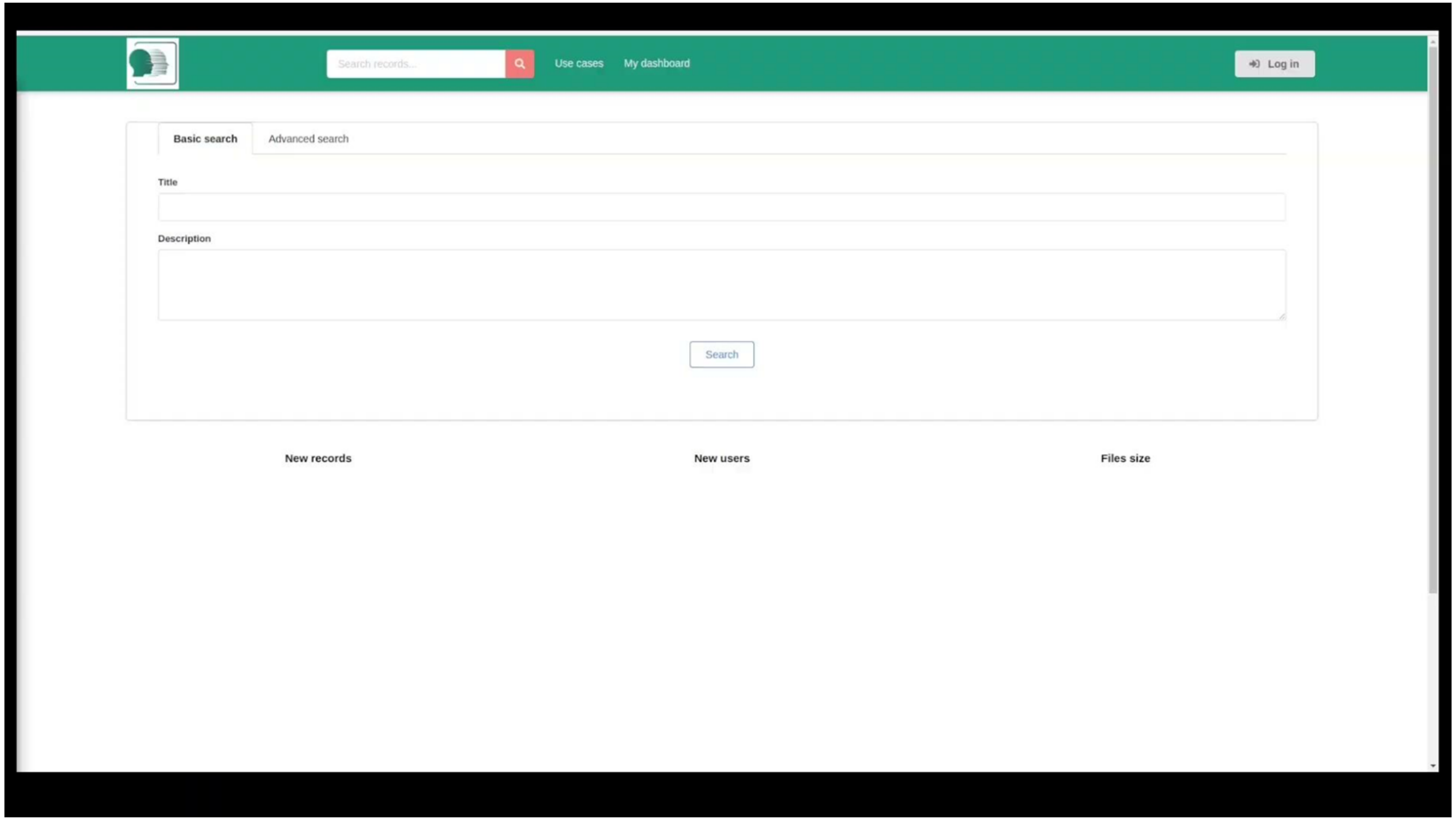
Creating an account...

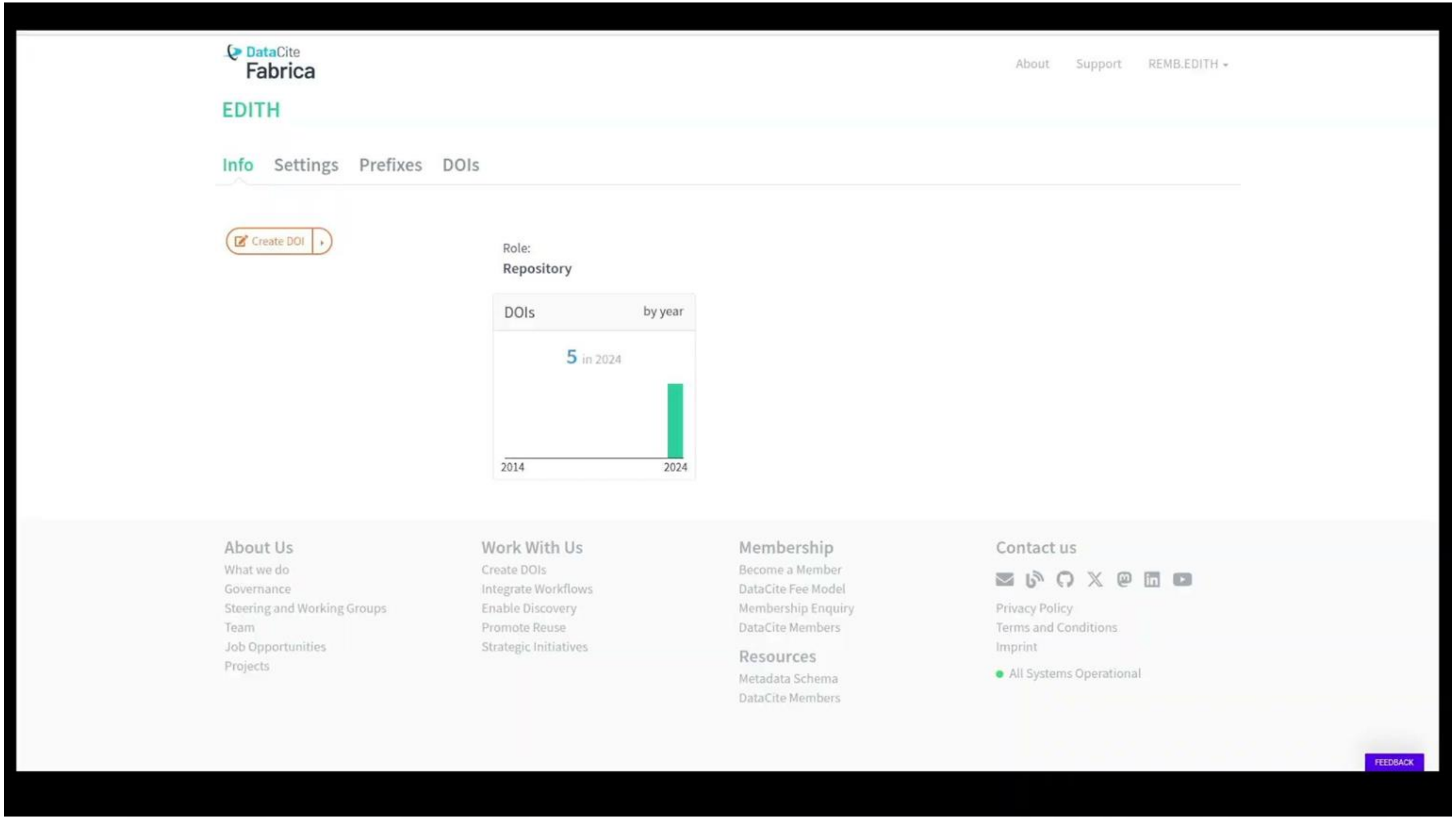


- Data Access and Utilization:
  - Accessing Comprehensive Data Sets
  - Cross-Referencing Data: researchers can cross-reference information, identify correlations
- Data Acquisition and Management Tools:
  - Databases and Data Warehouses: For storing and managing large volumes of medical, genetic, and behavioral data.
  - Data Integration Tools: For integrating data from various sources such as clinical records, genomic data, and wearable devices.
  - Data Security and Privacy Tools: To ensure that sensitive health data is protected and compliant with regulations like GDPR and HIPAA.
  - Data transformation services: data/input/output mapping services for a given standard

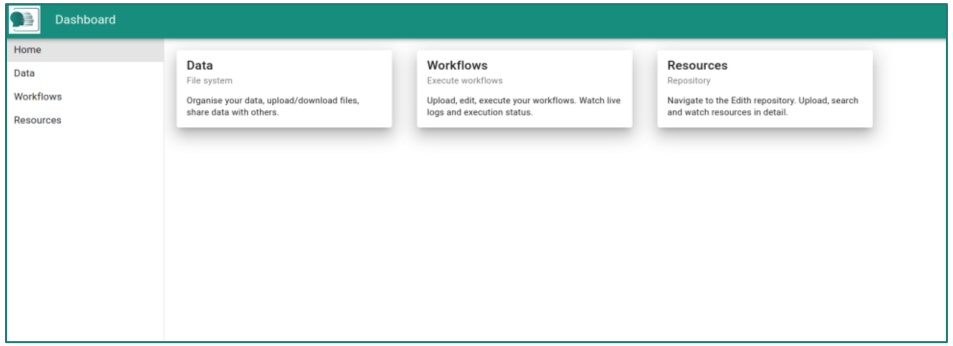
Working with CWL



Creating DOI



Collaborative Research



Sharing Models and Data: Collaborate with other researchers by sharing virtual models, data, and findings

Standardizing Research: Use standardized models and data

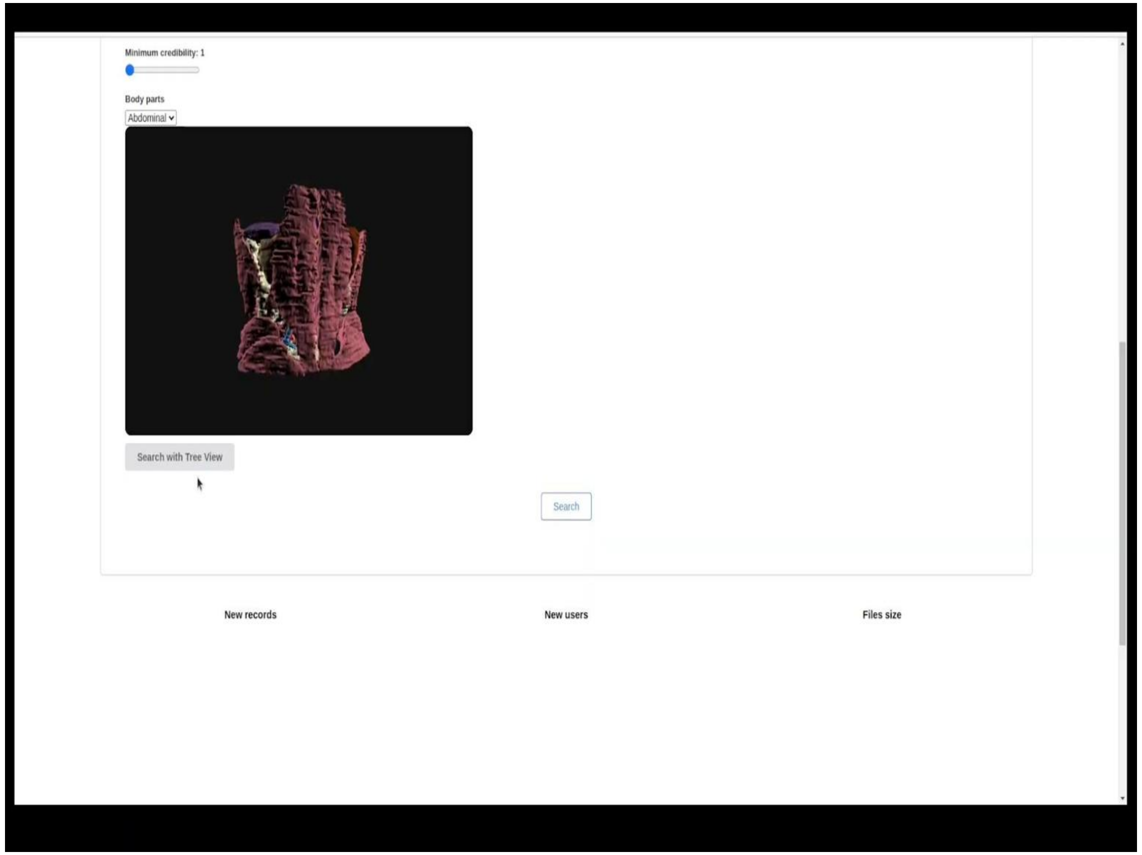
Version Control Systems: To manage code and data changes (e.g., Git, GitHub).

Collaboration Platforms (e.g., Jupyter Notebooks, Workflows engine).

Modeling and Simulation: Running Simulations
Personalized Simulation

Improved UX

- Visualization Tools:
  - Data Visualization Tools: To create interactive charts and graphs
  - 3D Visualization Software: For rendering and interacting with complex anatomical and physiological models



- Access to High-Performance Computing (HPC) Systems

Communities

Martin Golebiewski, Heidelberg Institute for Theoretical Studies

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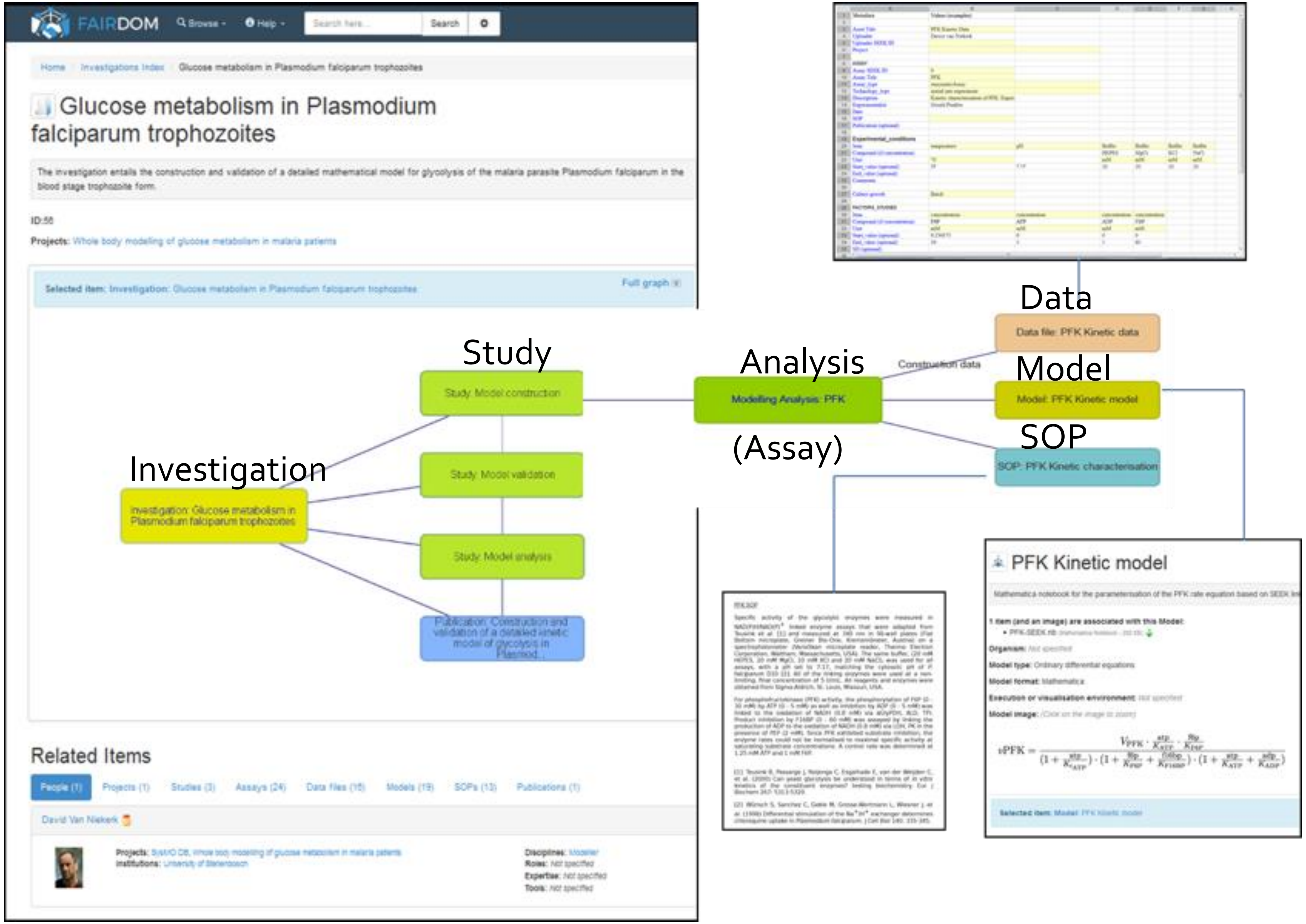
Integrative Data Management Systems: e.g. FAIRDOM SEEK



Wolstencroft K, Krebs O, Snoep JL, Stanford NJ, Bacall F, Golebiewski M, Kuzyakiv R, Nguyen Q, Owen S, Soiland-Reyes S, Straszewski J, van Niekerk DD, Williams AR, Malmström L, Rinn B, Müller W, Goble C: **FAIRDOMHub: a repository and collaboration environment for sharing systems biology research.** *Nucleic Acids Research 45(D1): D404-D407 (2017).* DOI: 10.1093/nar/gkw1032

Wolstencroft K, Owen S, Krebs O, Nguyen Q, Stanford NJ, Golebiewski M, Weidemann A, Bittkowski M, An L, Shockley D, Snoep JL, Mueller W, Goble C: **SEEK: a systems biology data and model management platform**. *BMC Systems Biology, 9: 33 (2015).* DOI: 10.1186/s12918-015-0174-y

Communities

Sofia Karvounari, ATHENA research center

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Required Adaptations

```json
{
    "$schema": "http://json-schema.org/draft-07/schema#",
    "additionalProperties": false,
    "id": "local://records/record_model_extended.json",
    "properties": {
        "$schema": {
            "$ref": "local://definitions-v1.0.0.json#/$schema"
        },
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            "properties": {
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                },
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                    "type": "string"
                },
                "credibility": {
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                },
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                    "type": "string"
                },
                "scale": {
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                    "type": "string"
                },
                "standard": {
                    "description": "The model standard, if applicable.",
                    "type": "string"
                }
            },
            "type": "object"
        }
    },
    "title": "EDITH Record Model Schema",
    "type": "object"
}
```

```json
{
    "$schema": "http://json-schema.org/draft-07/schema#",
    "id": "local://records/record_model_extended.json",
    "properties": {
        "$schema": {
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                }
            },
            "type": "object"
        }
    },
    "title": "EDITH Record Model Schema",
    "type": "object"
}
```

before → **after**

Enhanced Data Privacy and Security:

- Decentralized Data Storage: data remains within the local environment of each participating entity
- Data Sovereignty: Institutions retain control over their data, ensuring compliance with local regulations and policies

Enhanced Data Diversity and Quality:

- Aggregation of Diverse Datasets: integration of data from various sources, resulting in a richer and more diverse dataset
- Minimization of Bias: mitigate biases from localized data sets.

Interoperability and Standardization:

- Common Standards and Protocols
- Best Practices Sharing

Benefits

Scalability and Resource Optimization:

- Distributed Computing Resources: computational power and storage capacity of all participating nodes
- Cost Efficiency: distributed maintenance and infrastructure costs

Accelerated Research and Innovation:

- Collaborative Research: sharing insights and findings while maintaining control over their local data
- Faster Validation and Replication: innovations quickly validated and replicated

Benefits

Enhanced Personalization and Precision

Localized Adaptation: VHT models can be tailored to reflect the specific characteristics and needs

Real-Time Data Updates: Localized data continuously updated

Compliance with Ethical and Regulatory Standards

Local Ethical Oversight: compliance with local ethical guidelines and regulatory requirements

Regulatory Compliance: easy adaptation to various national and international regulations

Benefits

Resilience and Redundancy	System Redundancy: the failure of one node does not compromise the entire infrastructure Disaster Recovery: Data and tasks can be redistributed
Community and Stakeholder Engagement	Stakeholder Involvement: More active role for local communities and stakeholders
Innovation and Customization	Tailored Solutions developed by the different nodes

Industry

Mariano Vázquez, ELEM

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VIRTUAL HUMAN TWINS: THE FUTURE OF MEDICINE NOW

SUPERCOMPUTER-BASED VIRTUAL HUMANS

MARIANO VÁZQUEZ
ELEM BIOTECH

ELEM
THE VIRTUAL
HUMANS FACTORY

A SPINOFF COMPANY

BSC Barcelona Supercomputing Center
Centro Nacional de Supercomputación

A VIRTUAL HUMAN'S PLATFORM

SUPERCOMPUTING **EFFICIENCY**

\+

ACCURATE MULTISCALE / MULTIPHYSICS **MODELLING**

\+

VIRTUAL **POPULATION** GENERATION

SUPERCOMPUTER BASED **IN-SILICO CLINICAL TRIALS**
TO OPTIMIZE AND **PERSONALIZE** MEDICAL THERAPIES

A VIRTUAL HUMAN'S PLATFORM

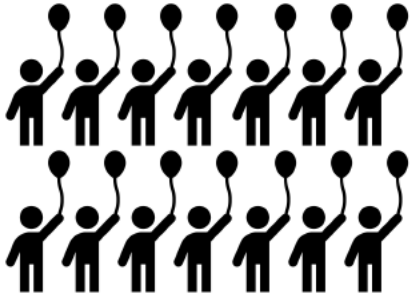
CLOUD DEPLOYED
(HYBRID: BACKEND + HPC INSTANCES)

ACCESSED THROUGH A WEB APP
TO SETUP THE CASE AND ANALYZE THE RESULTS

SECURED ACCESS

IN-SILICO CLINICAL TRIALS

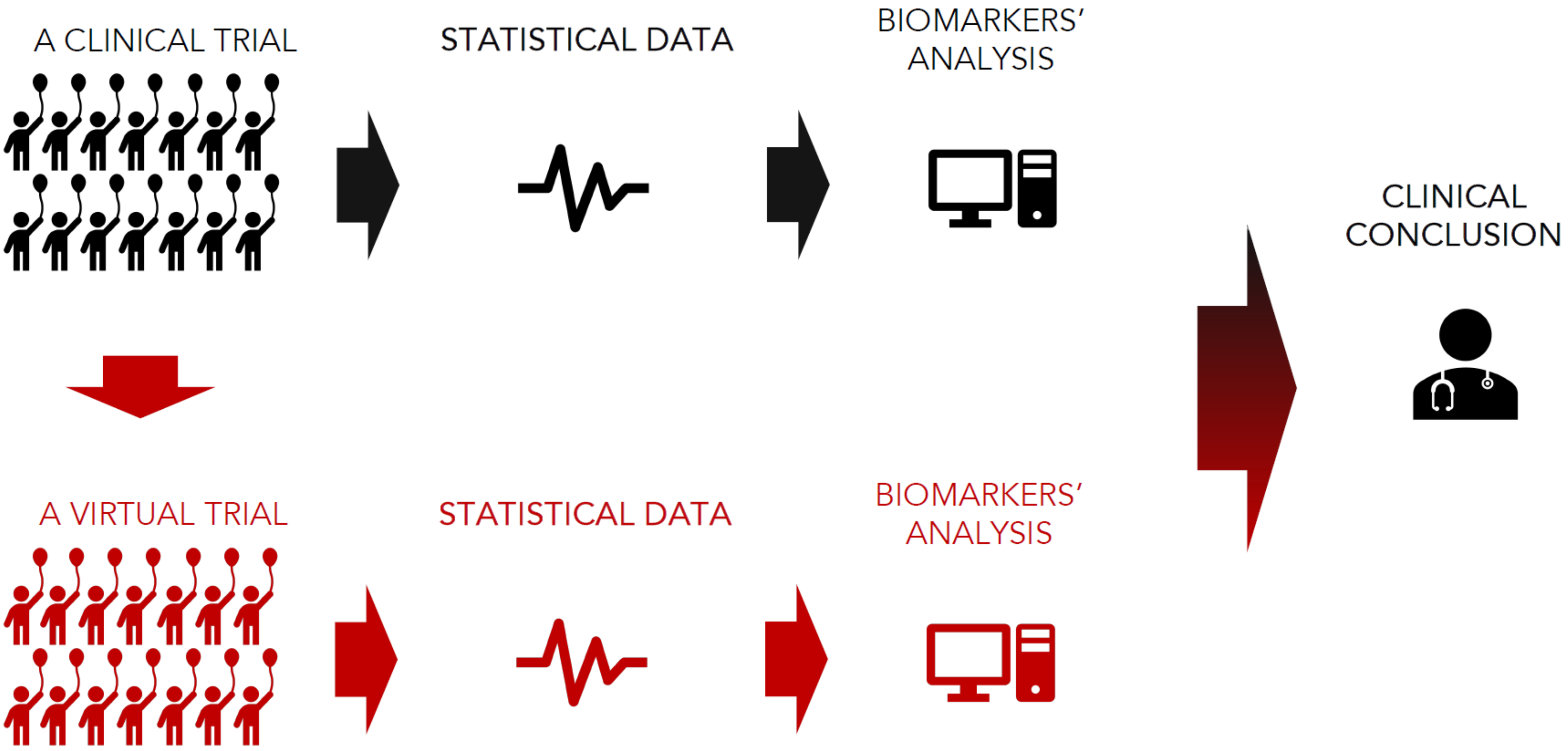
A CLINICAL TRIAL



CLINICAL
CONCLUSION

IN-SILICO CLINICAL TRIALS

IN-SILICO CLINICAL TRIALS



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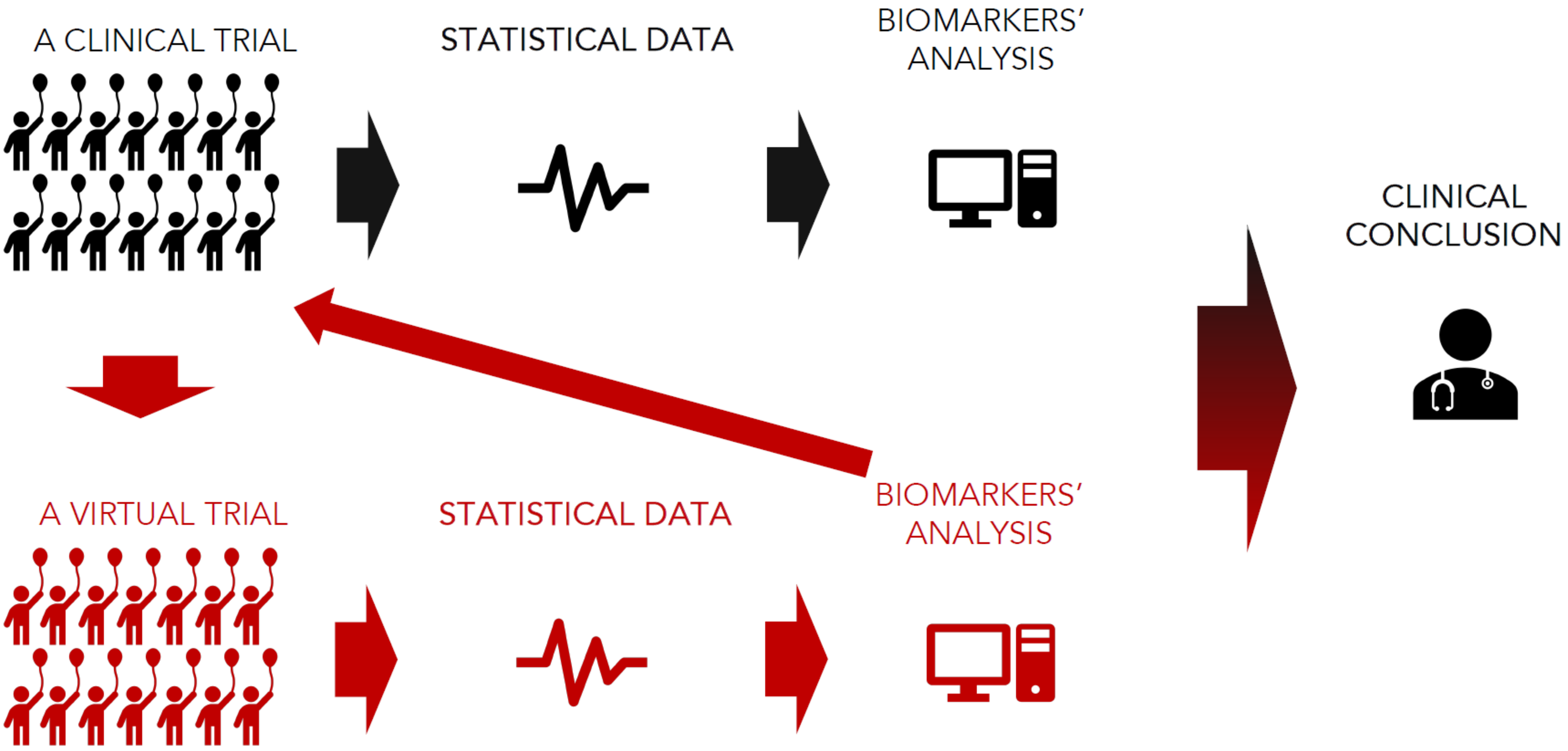
IN-SILICO CLINICAL TRIALS



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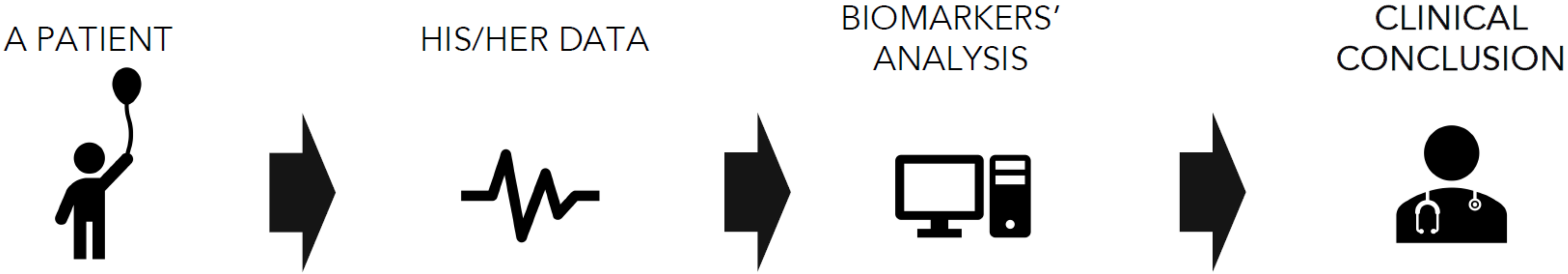
PRECISION MEDICINE

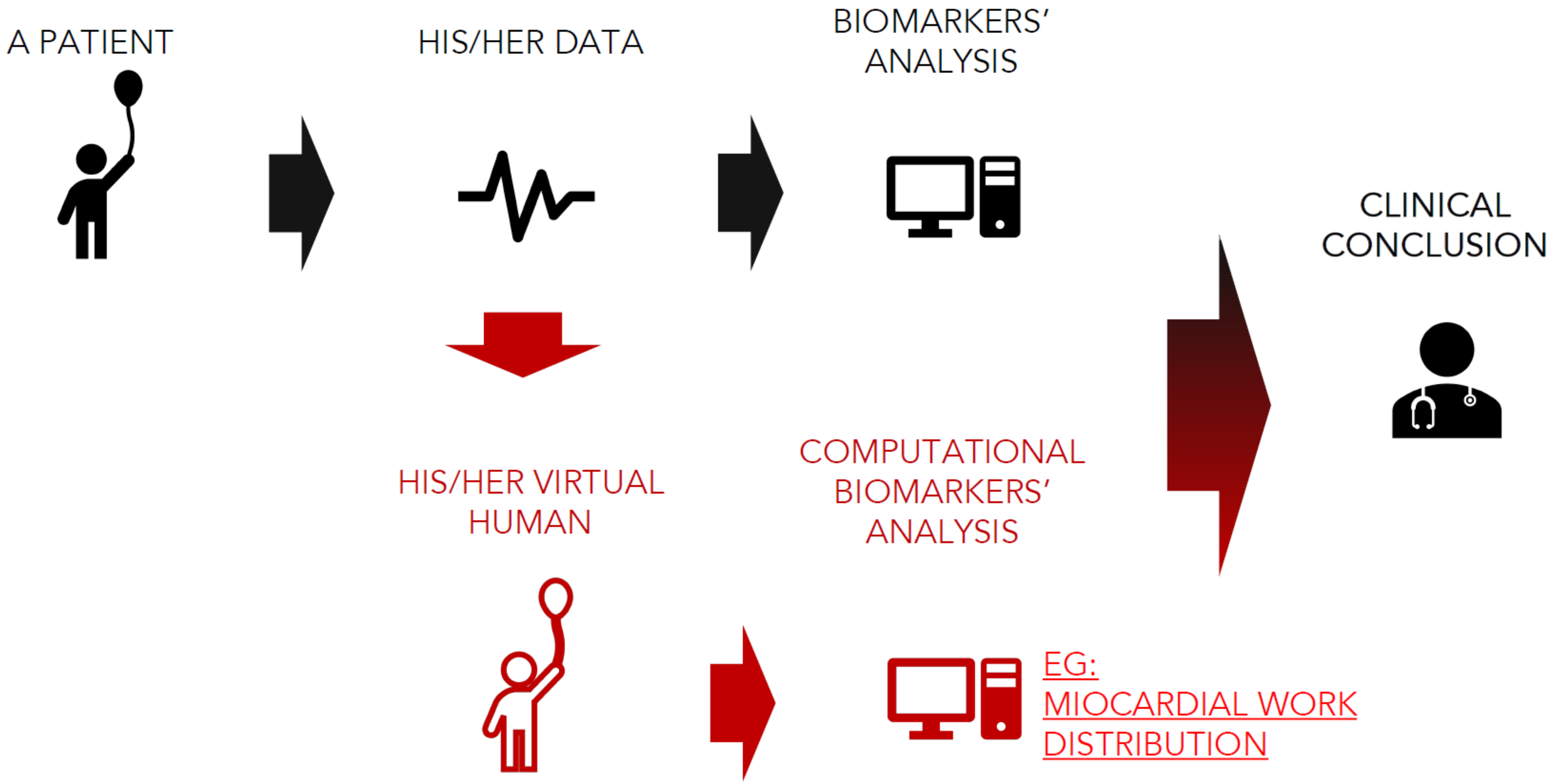
A PATIENT

CLINICAL
CONCLUSION

PRECISION MEDICINE



PRECISION MEDICINE



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THE CARDIOVASCULAR SYSTEM

COLLABORATORS:

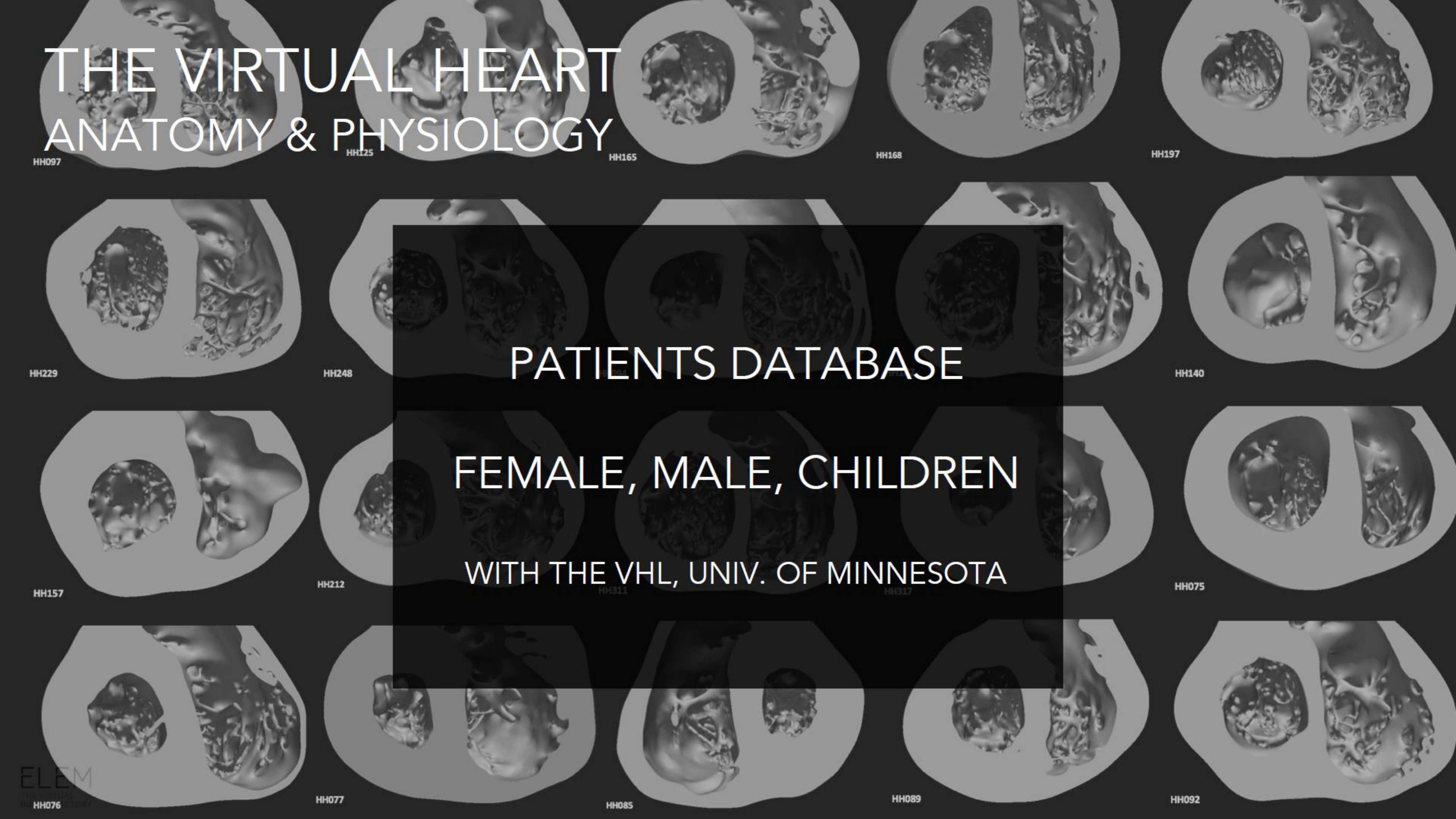
THE VISIBLE HEART LAB - UNIV. OF MINNESOTA (US)
CENTRO NACIONAL DE INVESTIGACION CARDIOVASCULAR (SPAIN)
HOSPITAL DE SANT PAU (SPAIN)
UNIVERSITY OF OXFORD (UK)
UNIVERSITAT POMPEU FABRA (SPAIN)
UNIVERSITAT POLITECNICA DE VALENCIA (SPAIN)
GEORGE MASON UNIVERSITY (US)
UNIVERSITY COLLEGE LONDON (UK)
SAN DIEGO STATE UNIVERSITY (US)
MEDTRONIC (US)
BOEHRINGER INGELHEIM (D)
FDA (US)

THE VIRTUAL HEART
ANATOMY & PHYSIOLOGY

PATIENTS DATABASE

FEMALE, MALE, CHILDREN

WITH THE VHL, UNIV. OF MINNESOTA



THE VIRTUAL HEART
ANATOMY & PHYSIOLOGY

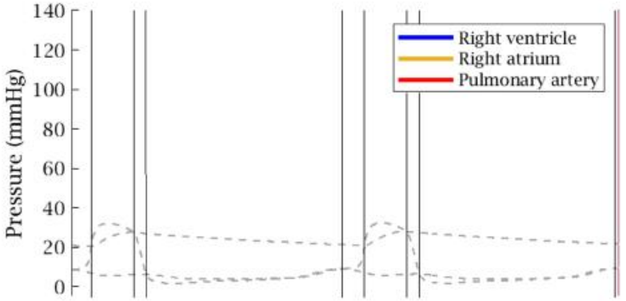
VIRTUAL
PATIENTS DATABASE

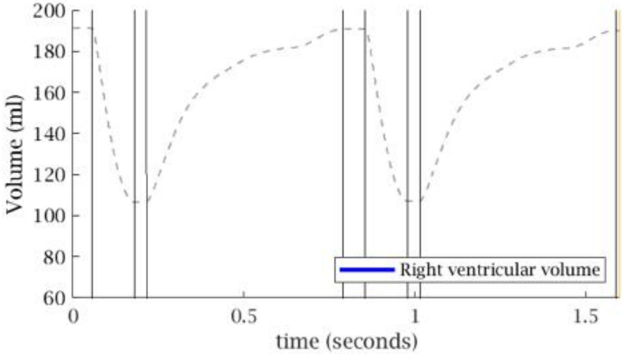
FEMALE, MALE, CHILDREN

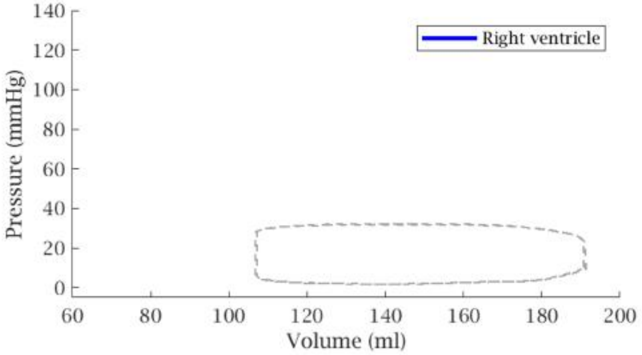
HEALTH, DISEASE &
TREATMENT

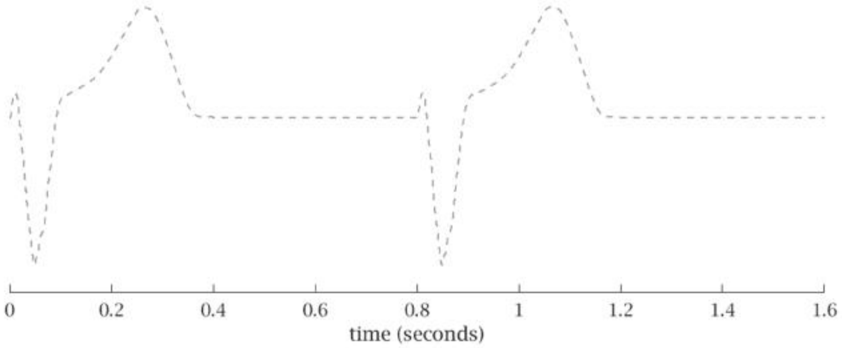
Cardiac modelling

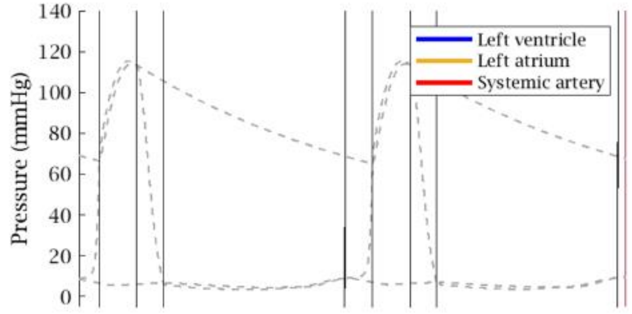
25-years old female healthy volunteer

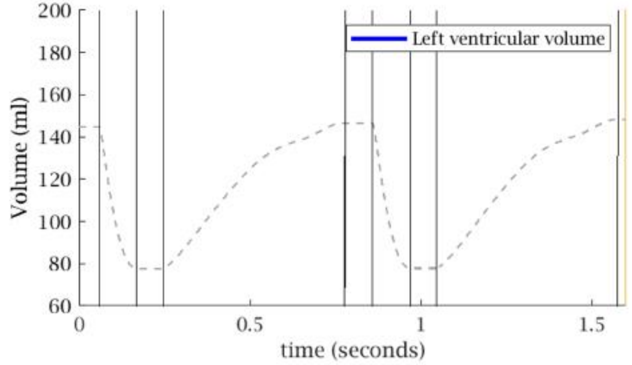


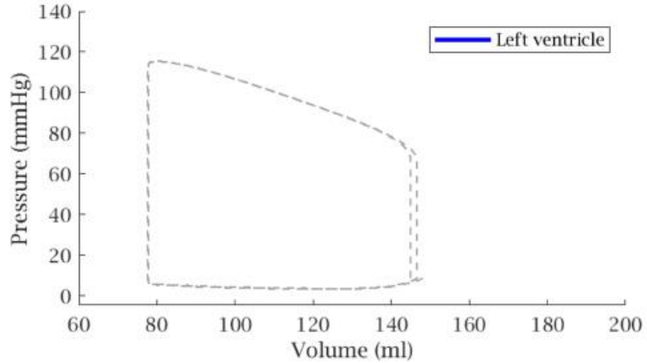


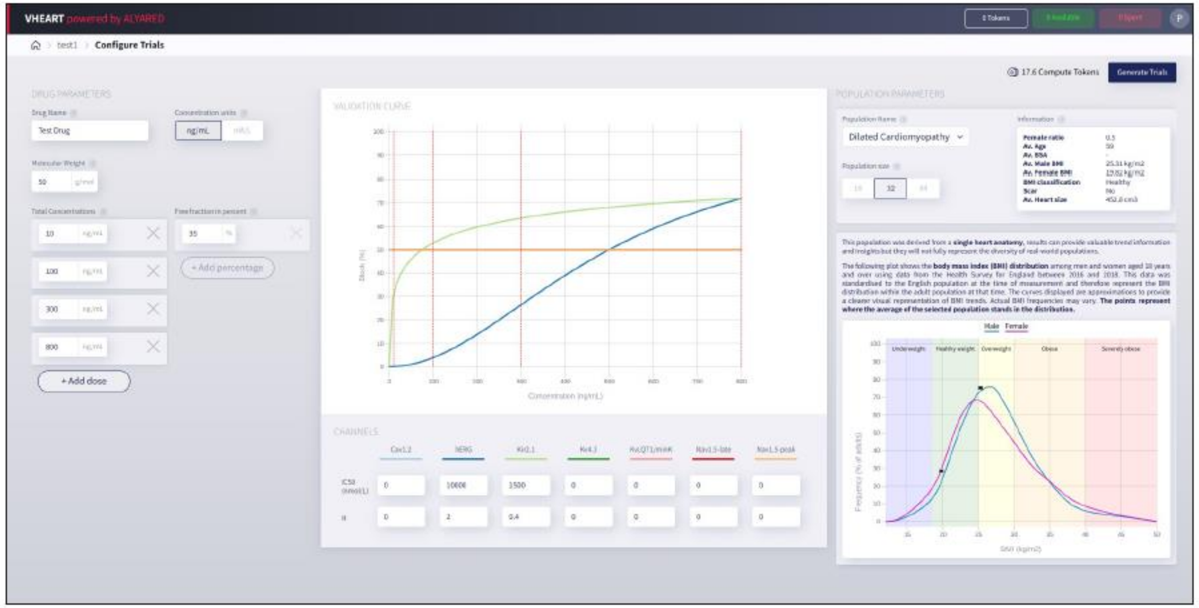












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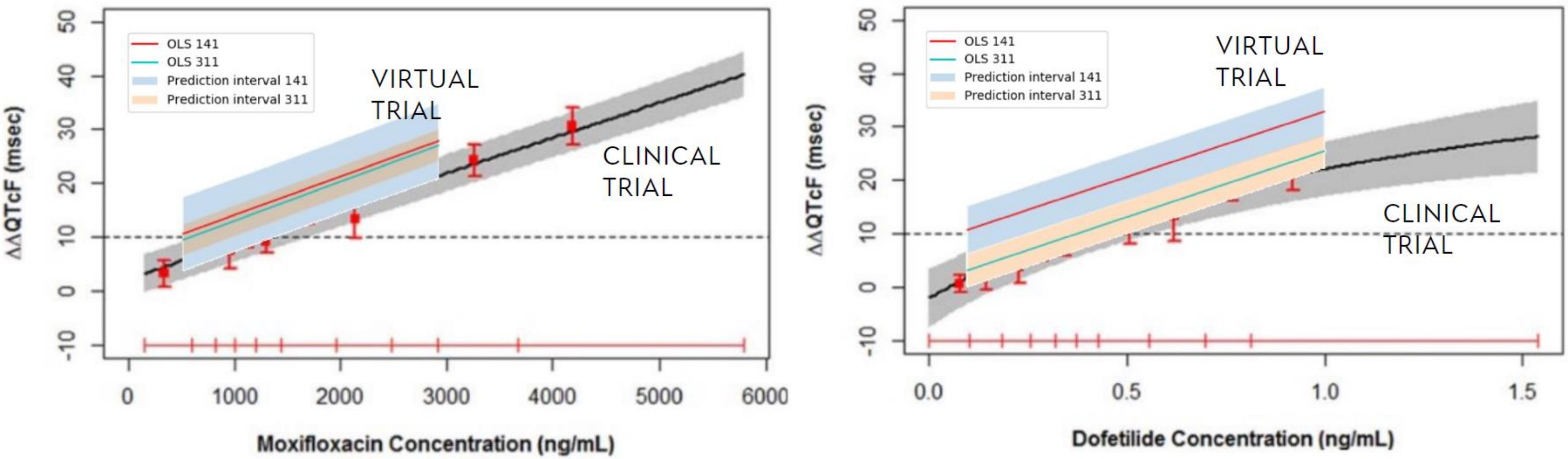
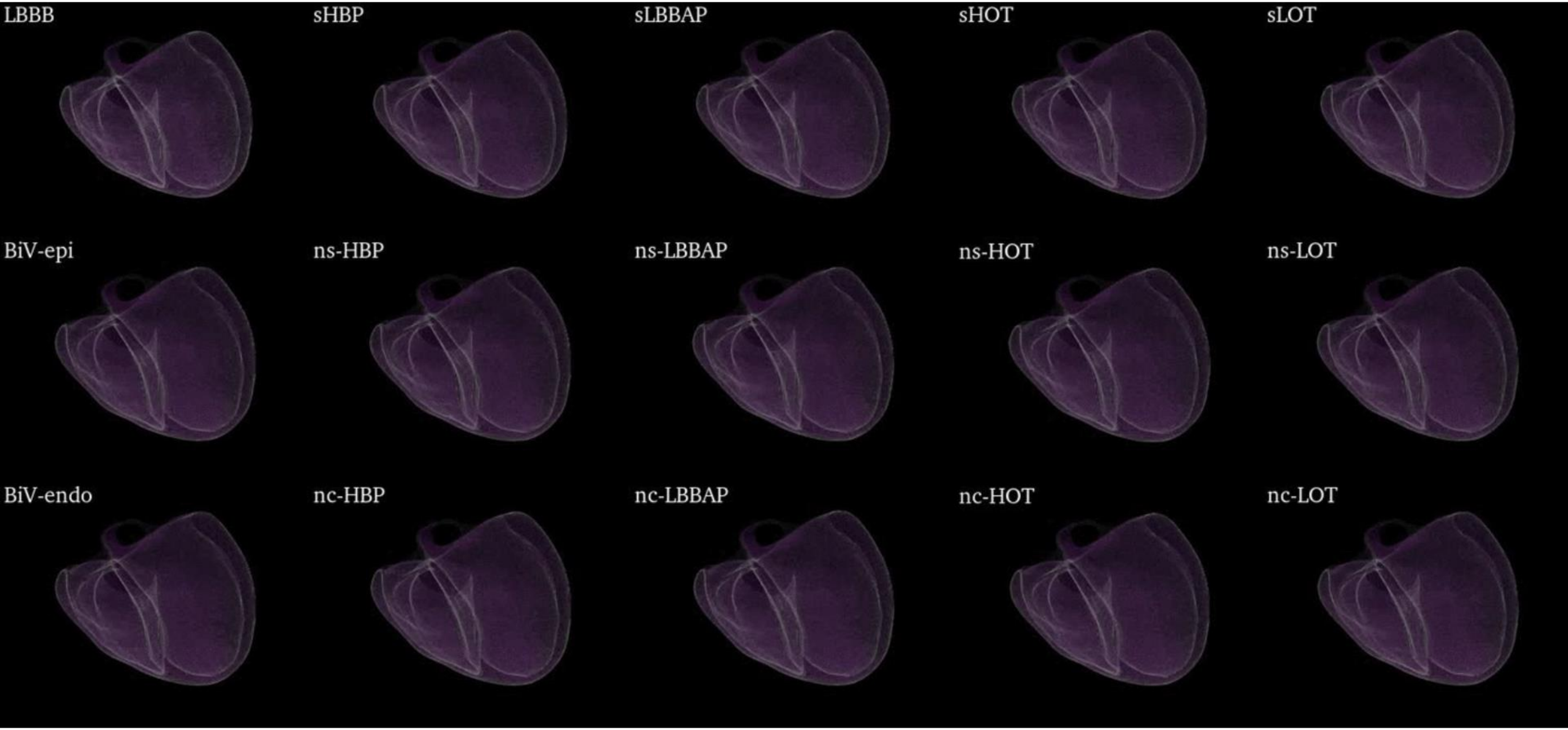
HUMAN CARDIAC IN-SILICO CLINICAL TRIAL PIPELINE FOR CARDIAC SAFETY ASSESSMENT



VIRTUAL CLINICAL QT EXPOSURE-RESPONSE STUDIES – A TRANSLATIONAL COMPUTATIONAL APPROACH
AGUADO-SIERRA ET AL.
JOURNAL OF PHARMACOLOGICAL AND TOXICOLOGICAL METHODS, 2024

ELEM THE VIRTUAL HUMANS FACTORY

CRT ASSESSMENT THROUGH PERSONALIZATION



CONCLUSION

ELEM BIOTECH IS THE VIRTUAL HUMANS FACTORY

THE FUTURE NOW

THANKS!

VIRTUAL HUMAN TWINS: THE FUTURE OF MEDICINE NOW

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A SPINOFF COMPANY

Barcelona Supercomputing Center
Centro Nacional de Supercomputación

ELEM
THE VIRTUAL HUMANS FACTORY

European Innovation Council

Disc4All

VITAL

CompBioMed

Industry

Evita Mailli, ATHENA research center

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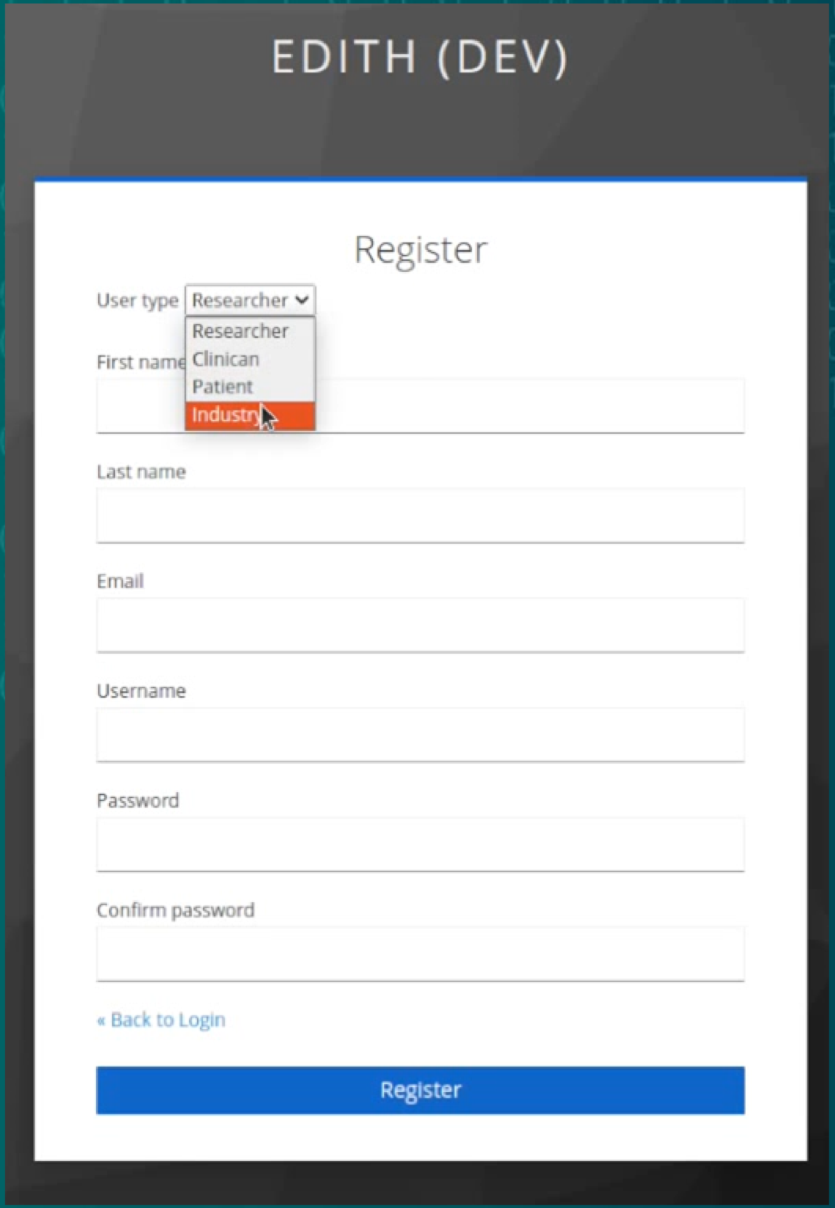
Industry



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How

Data Anonymization and Aggregation

Anonymized Data

Aggregated Data (e.g. statistical analyses, trends, and summaries derived from their data)

Data Access Controls, Usage Policies

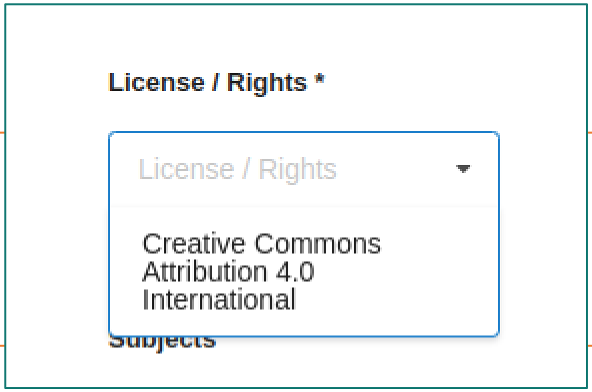
Controlled Access: different user roles - only authorized users can access specific datasets

Usage Policies: can restrict certain uses

Federated Learning

Federated Learning: data remains within the company's infrastructure, insights and models are shared

How



Partnerships and Licensing Agreements

- Licensing Models: grant access while retaining ownership and control
- Data Sharing Agreements: how data can be accessed, used, and shared

Contribution of Tools and Algorithms

- Proprietary Algorithms: used within the repository without revealing the underlying data or methodology (e.g., providing APIs)
- Open-Source Tools: Develop and share open-source tools, software, and algorithms

Benefit-Sharing Models

- Reciprocal Sharing: Implement benefit-sharing models where contributors receive access to other valuable data and tools in return for their contributions.
- Incentive Programs: reward companies for contributing valuable data and resources (e.g., access to exclusive research findings, recognition, financial incentives)

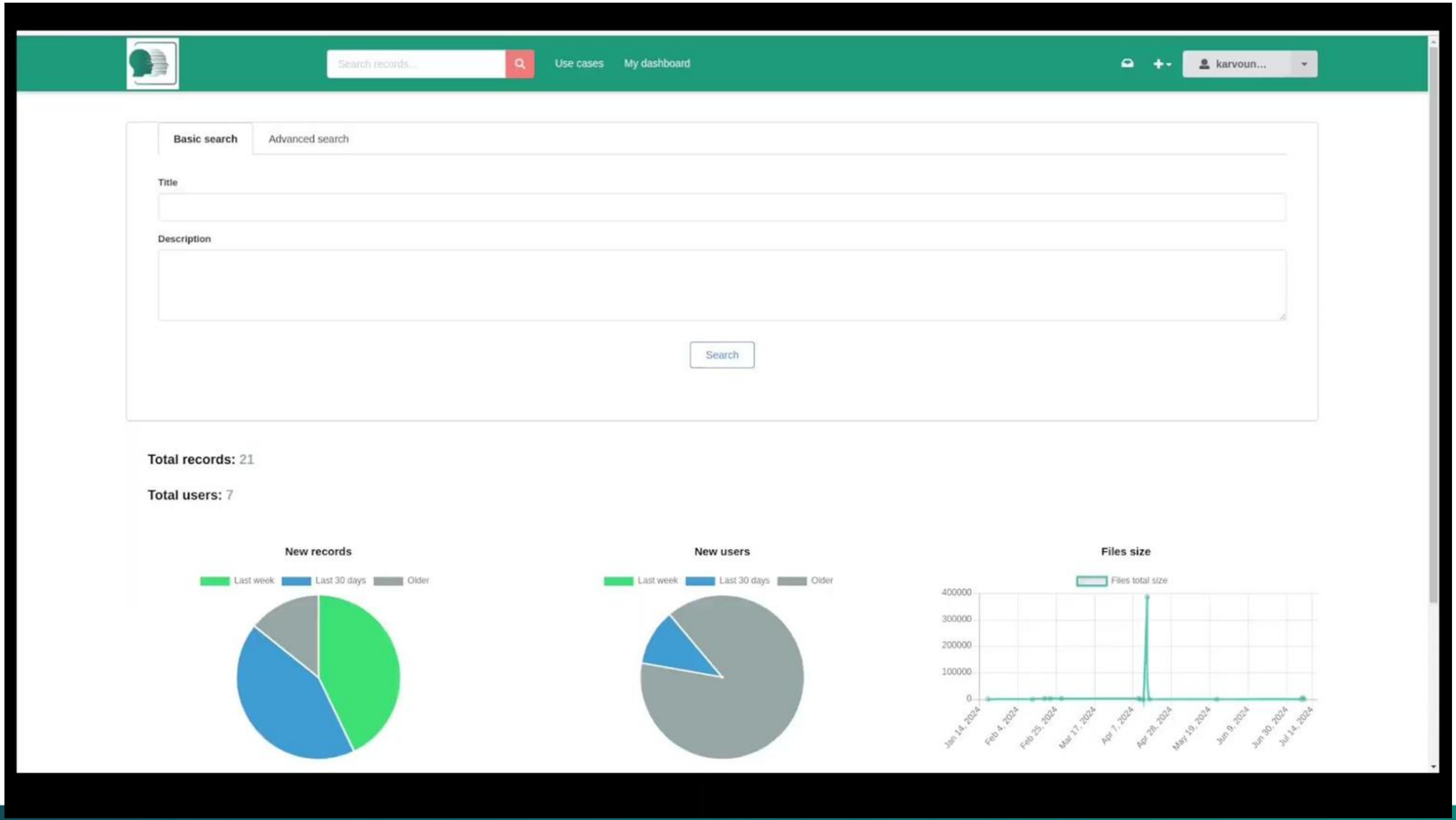
What

- Patient Data and Demographics
- Disease Models:
  - Disease Progression: Simulations of how different diseases progress over time in various demographic groups.
  - Pathophysiology: underlying mechanisms of diseases and how they affect different body systems.
- Pharmacokinetics and Pharmacodynamics:
  - Drug Interactions: how different drugs interact within the human body
  - Dosage Simulations: Models predicting the effects of different drug dosages on patients with varying characteristics.

What

- Clinical trial design
- Behavioral and Lifestyle Data:
  - Lifestyle Impact: Simulations showing how factors like diet, exercise, and smoking affect health outcomes.
  - Behavioral Health: Data on how mental health conditions and behavioral patterns influence physical health.
- Public Health Data:
  - Epidemiological Models: Simulations of disease spread and the impact of public health interventions.
  - Health Impact Assessments: Data assessing the potential health impacts of policy cges or environmental factors.

Use case oriented



Healthcare provider

Vincent Uyttendaele, InSiliCare and University of Liège

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Clinical Use Case
Glucose Control in Intensive Care

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Insilicare | University of Liège
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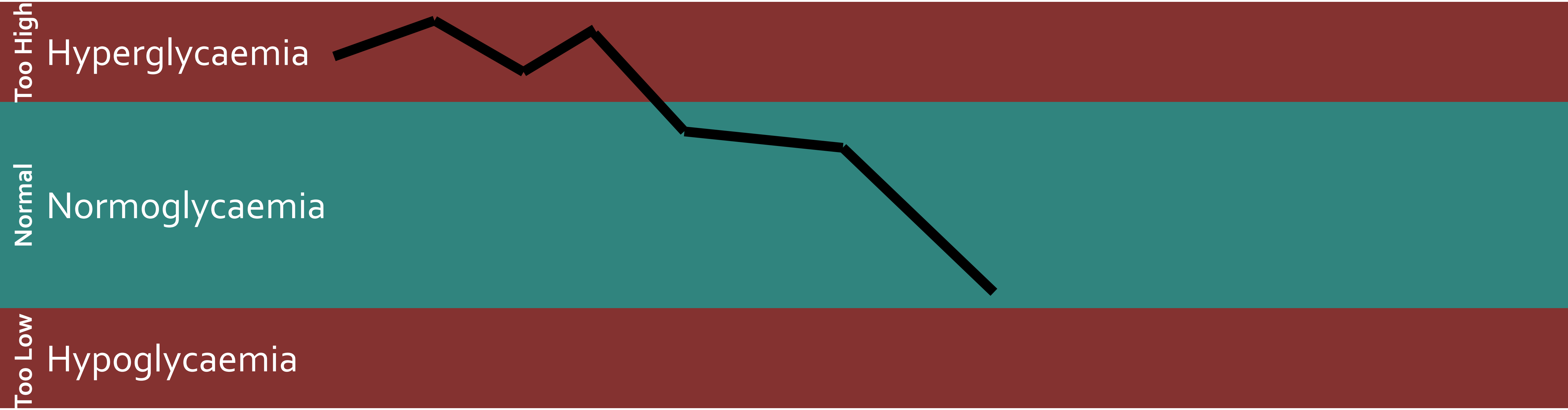
Glucose Control (GC) in the Intensive Care unit (ICU)

Hyperglycaemia occurs in 30-50% of ICU patients (with or without diabetes)

Too High	Hyperglycaemia increases risk of infection, morbidities, and death
Normal	Normoglycaemia is associated with improved outcomes and reduced mortality
Too Low	Hypoglycaemia lead to severe brain damage and death

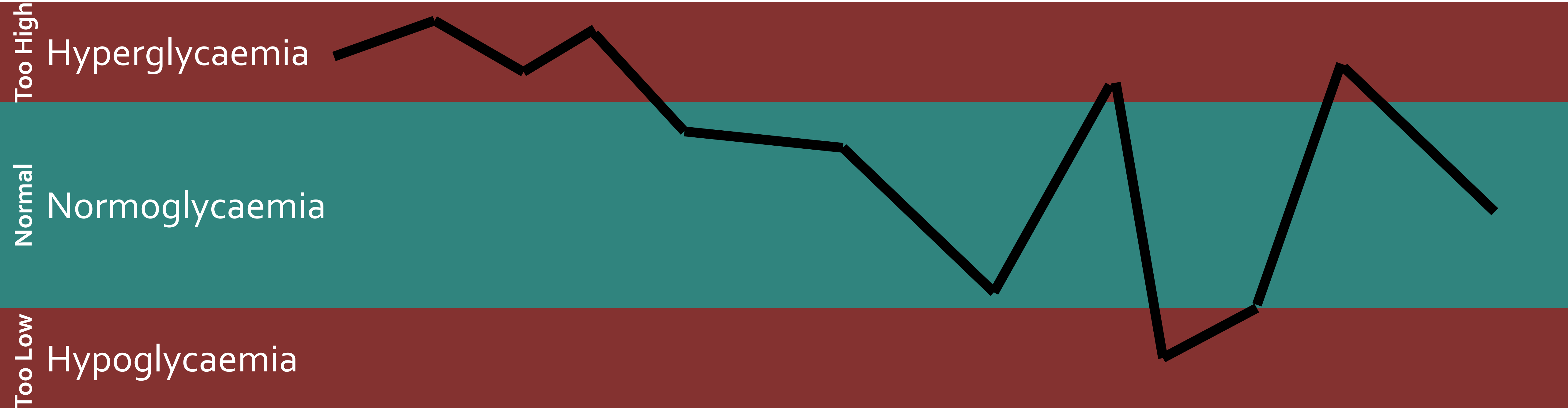
Glucose Control (GC) in the Intensive Care unit (ICU)

Insulin must be administered but **increases the risk of hypoglycaemia**



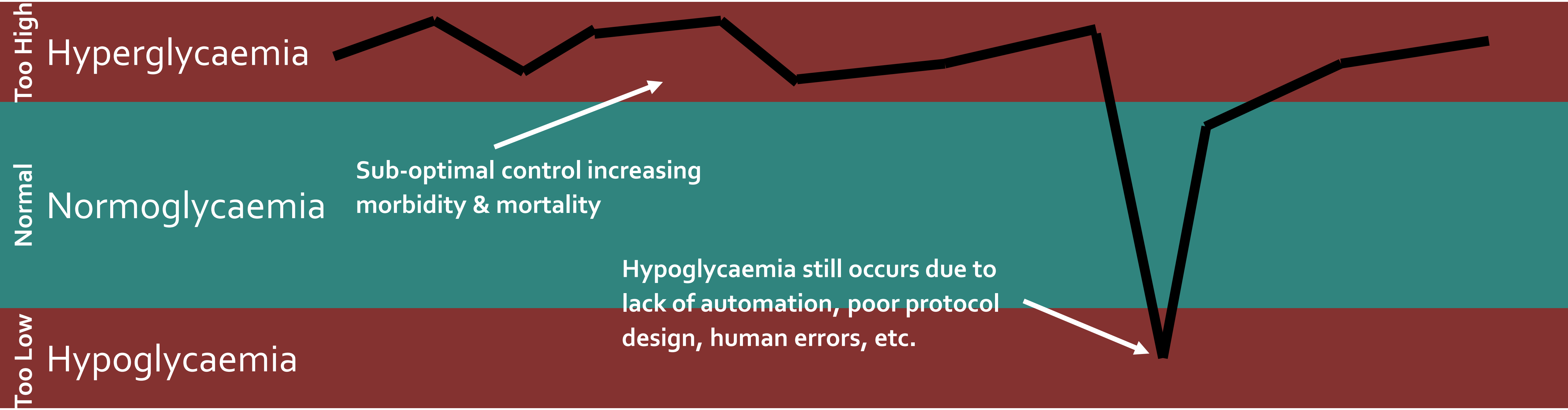
Glucose Control (GC) in the Intensive Care unit (ICU)

What makes GC hard is variability: **differ between patient & over time**

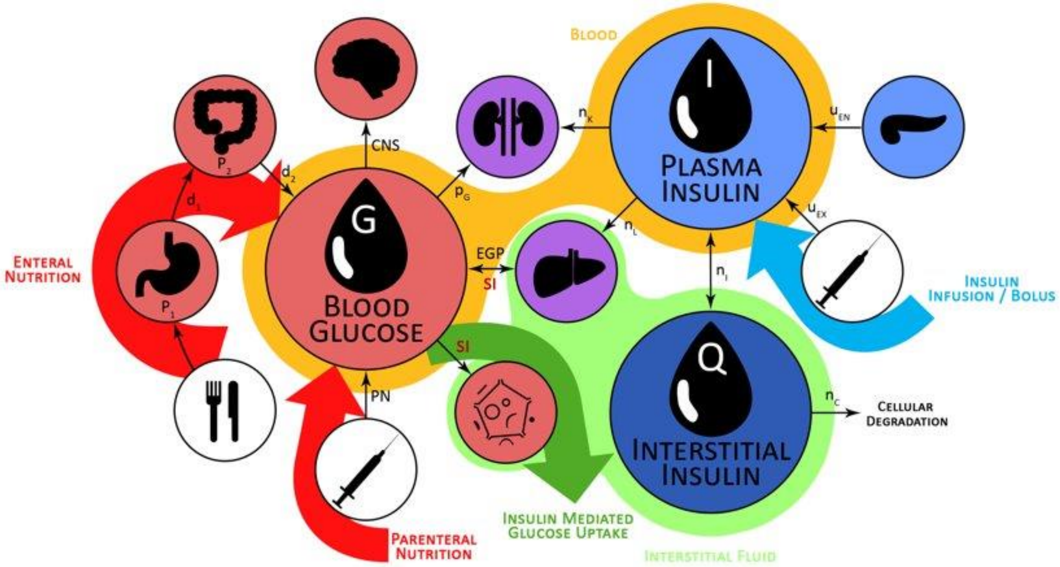


Glucose Control (GC) in the Intensive Care unit (ICU)

Permissive hyperglycaemia as a “**first do no harm**” approach



A Digital Twin Model of Glucose & Insulin dynamics to identify ‘variability’



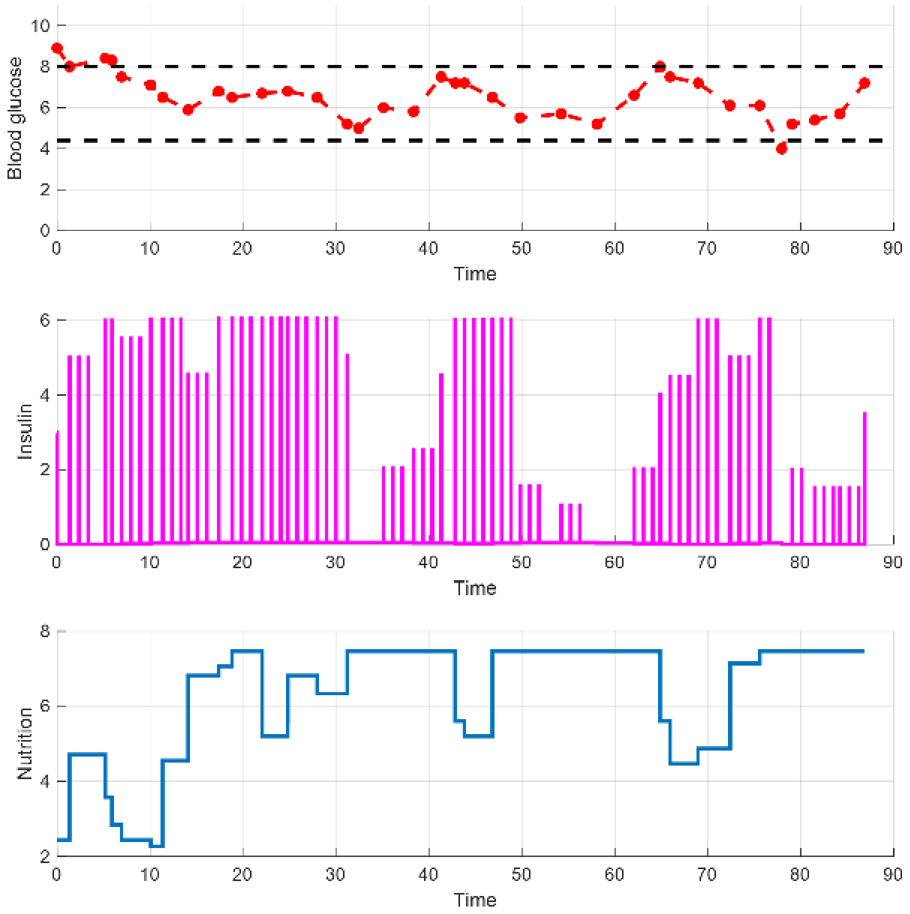
“White Box” model characterising pharmaco-dynamics and kinetics of glucose and insulin metabolic pathways

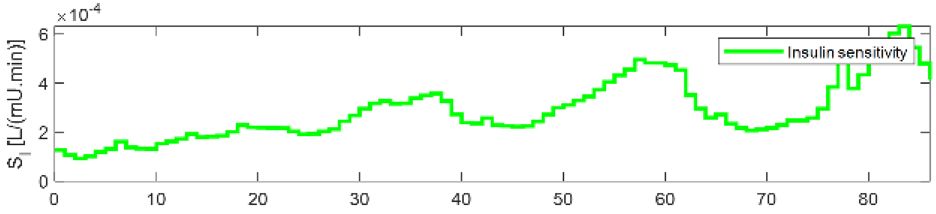
3 clinical inputs : Glucose, Insulin, Nutrition over time

Other inputs such as : diabete, age, sex, BMI

1 output : Insulin sensitivity (not / hardly measurable)

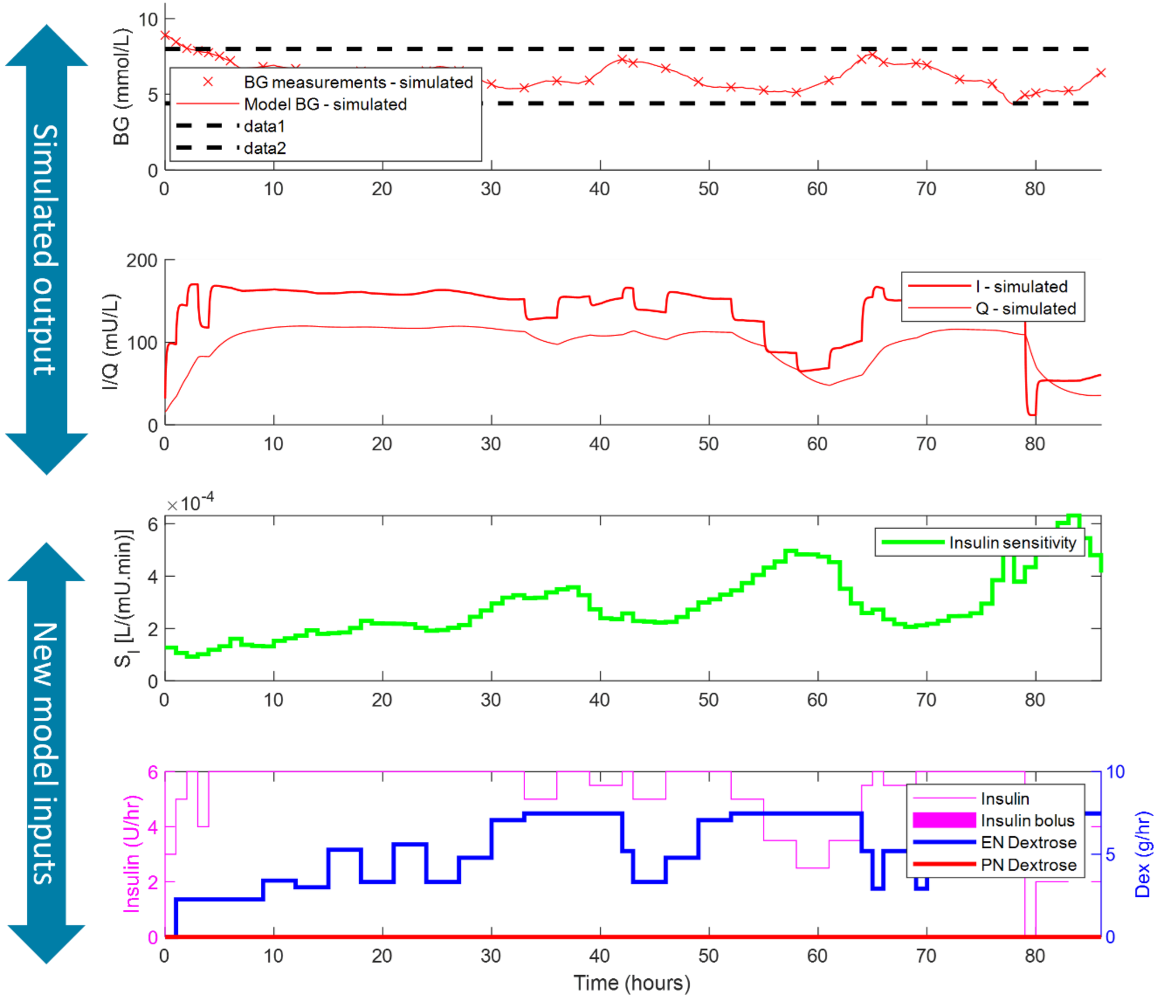
A Digital Twin Model of Glucose & Insulin dynamics to identify 'variability' in clinics





Patient-specific **insulin sensitivity profile** can be identified

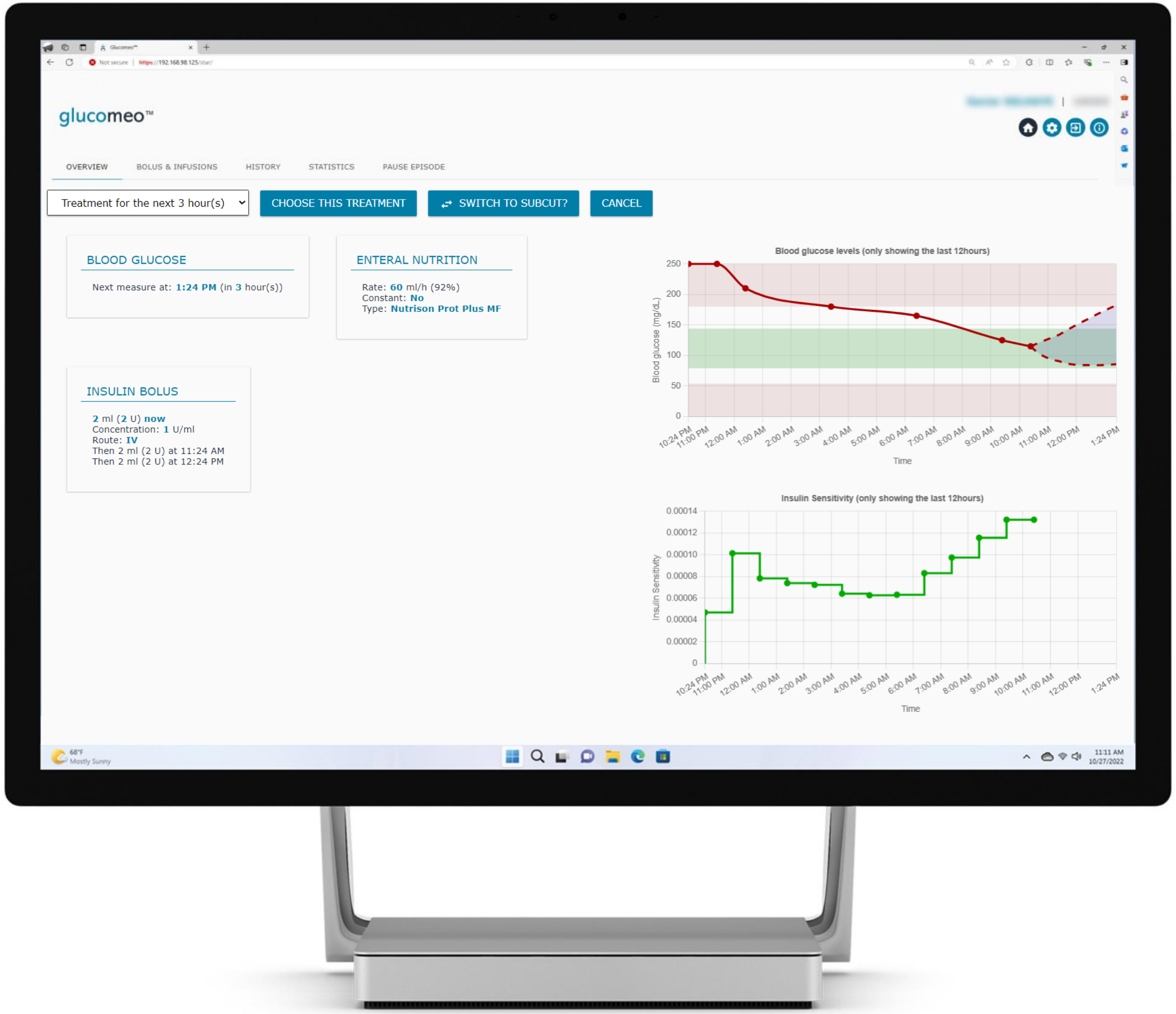
Application 1



Clinicians and Academics can use the model for individual / cohort analyses or in-silico trials

For example, safety assessment of new protocol design **prior clinical use**

Application 2



Clinical application:

use the model associated with **predictive AI** to personalise treatment by **assessing and balancing treatment risks** in real-time for clinical decision support at patient bedside

Gains

Application 2

Optimal GC and Nutrition improving safety and efficacy → Happy patients with improved outcomes

High protocol compliance, reduced clinical burden, and reduced human errors → Happy clinical staff

Improved patient management across nursing shifts and wards → Happy co-workers / streamline process

>5000€/patient reduction costs ! → Happy social security!

Thank you for the attention!

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Healthcare provider

Amaryllis Raouzaiou, Konstantinos Triantos, ATHENA research center

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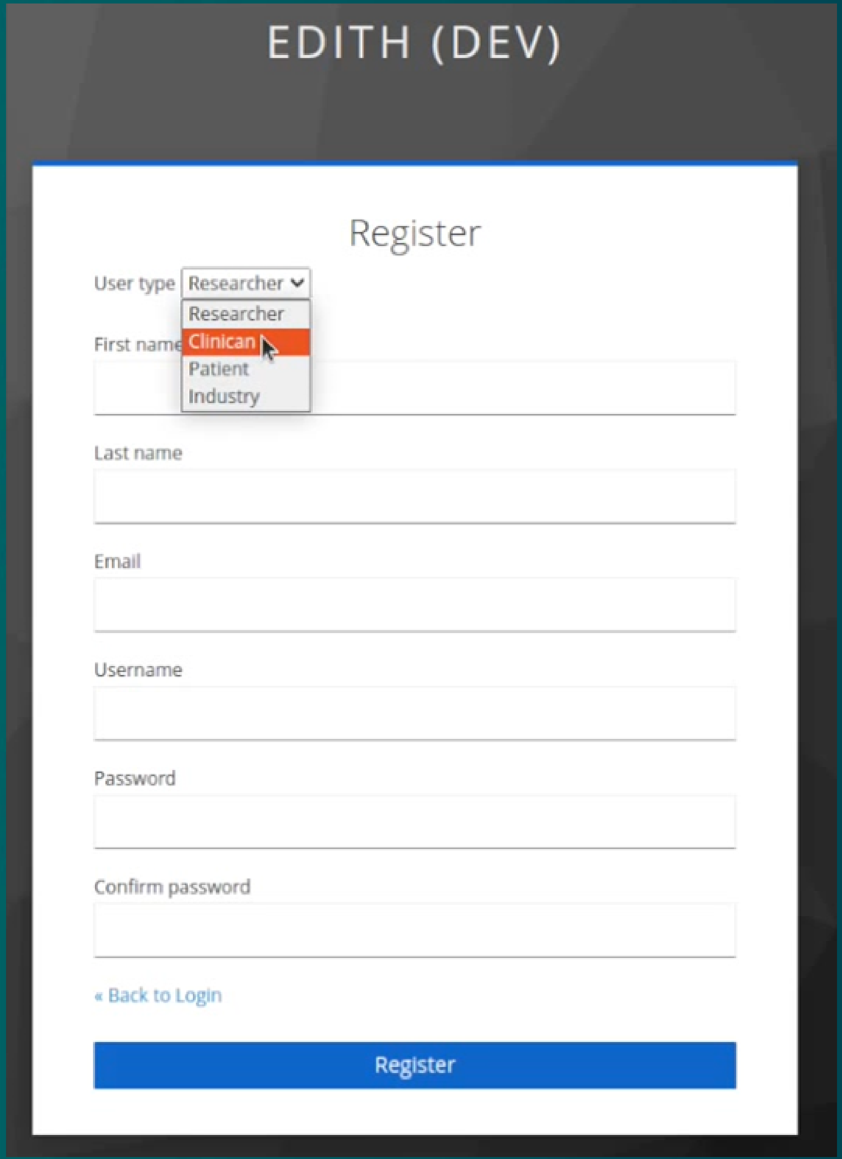
Healthcare provider
Clinician



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Criteria

Integration with Health IT Systems

EHR Integration: integration with EHR systems to allow easy access to patient data and insights.

Interoperability: compatibility with various health IT systems to facilitate smooth data exchange and integration.

User-Friendly Interfaces

Clinician Dashboards: intuitive interfaces for easy access to VHT insights and recommendations.

Data Security and Privacy

Compliance: with all relevant data protection regulations to maintain patient confidentiality.

Training and Support

Clinician Training Programs

Ongoing Support

Services

Personalized Patient Care

Individualized Treatment Plans and Predictive Analytics using precise virtual models.

Clinical Decision Support - Therapeutic Adjustments

Real-Time Data Integration with electronic health records (EHRs) to provide real-time insights (future work)

Advanced Imaging Interpretation

Dynamic Treatment Adjustment: test different therapeutic interventions virtually, adjusting treatments dynamically based on simulated outcomes.

Interdisciplinary Collaboration

Team-Based Care

Specialist Consultation

Monitoring and Follow-Up

Dynamic Monitoring: new patient data, monitor disease progression and treatment effectiveness

Remote Monitoring: telemedicine

Services

Modeling and Simulation

Running Simulations: Use the repository to run simulations on virtual human models to predict outcomes of medical treatments, understand disease progression, or evaluate surgical procedures without risking patient safety.

Personalized Simulations: Utilize individual-specific data from the repository to create personalized virtual human twins for precise medical research and customized treatment planning.

Research and Clinical Trials

Trial Outcomes: Results from previous clinical trials, including efficacy and safety data for various treatments.

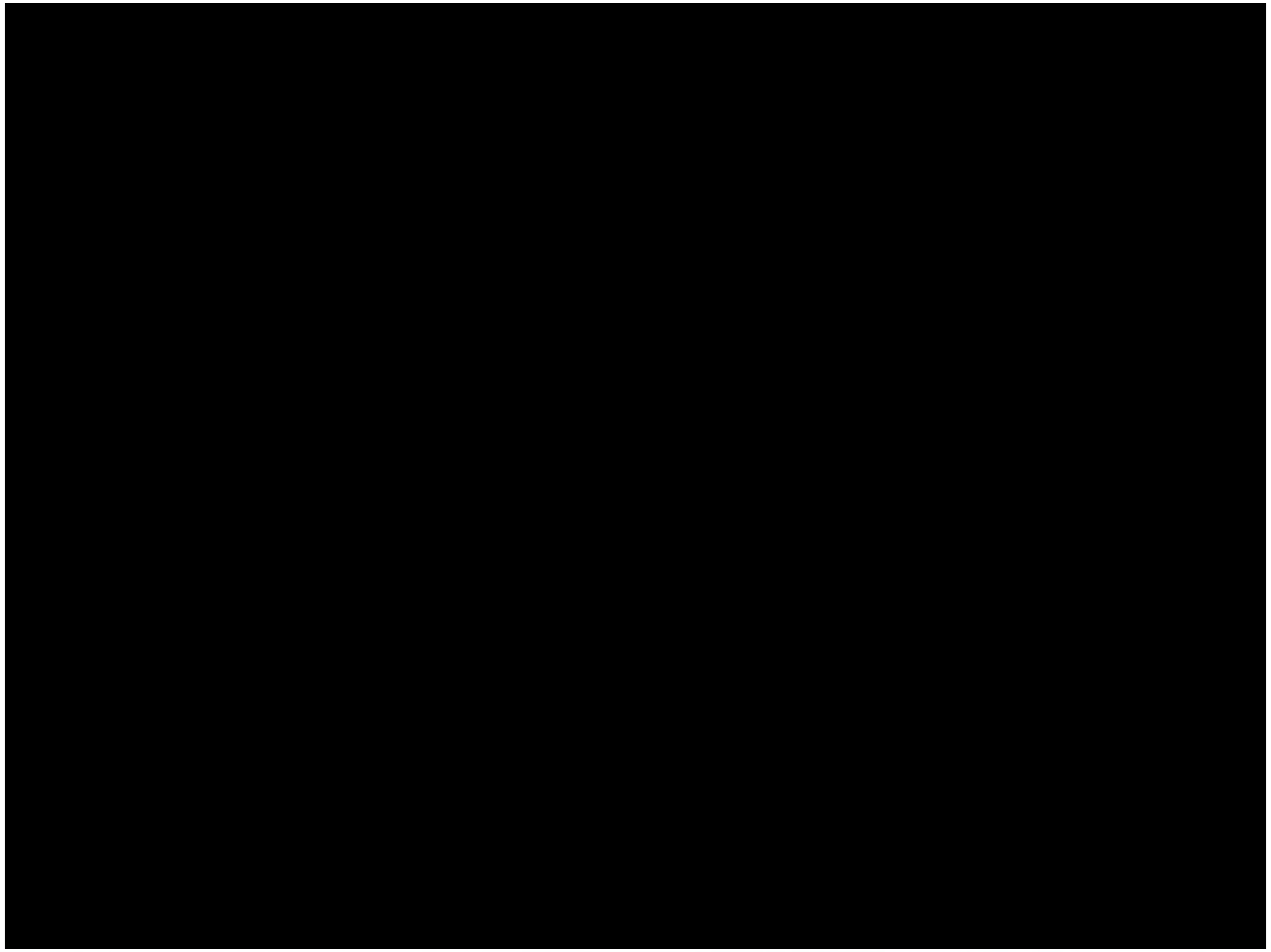
Patient Recruitment: Information on patient populations that participated in trials, helping to design future studies.

Training and Education

Clinician Training: rare or complex cases

Continuing Medical Education: latest medical advancements and techniques.

Running a Workflow



Patient

Sabato Mellone, University of Bologna
Amaryllis Raouzaiou, ATHENA research center

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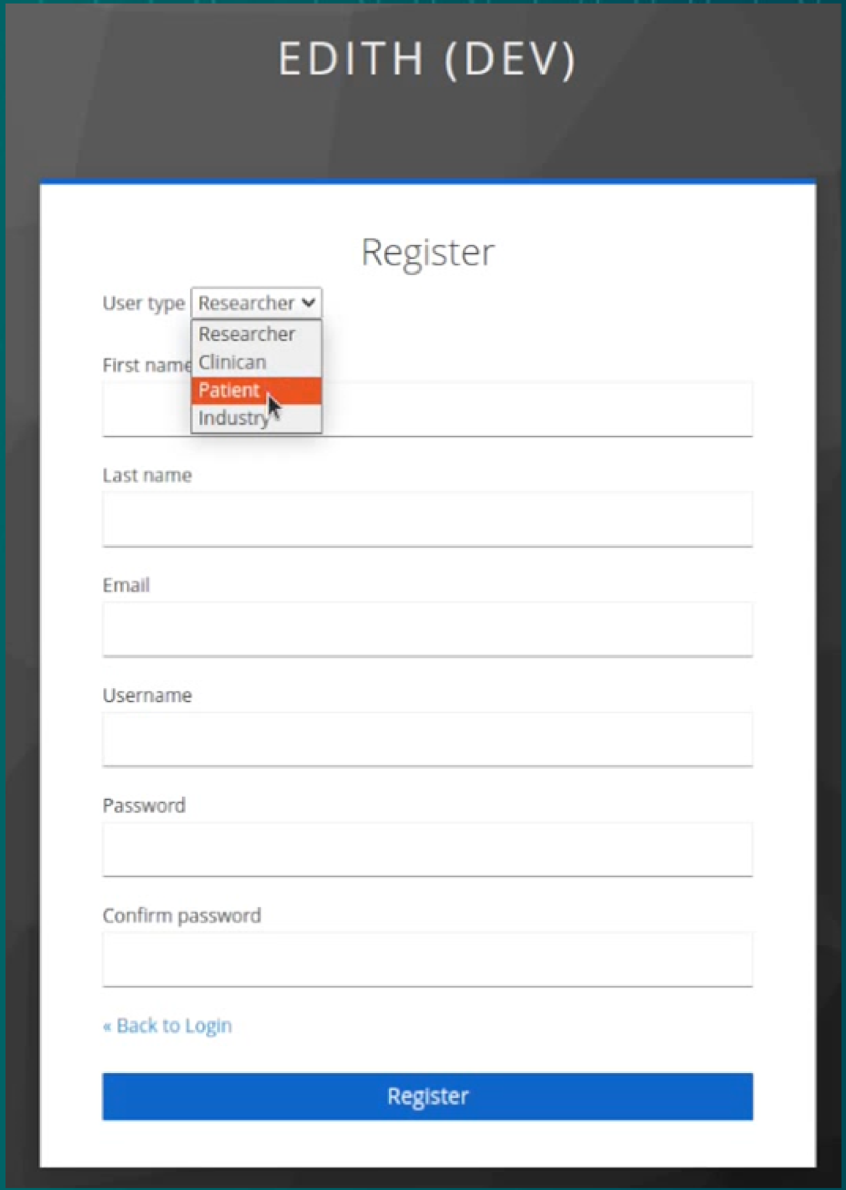
Patient



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Process

Registration and Access:

- Create an Account: separate "Patient" role
- Consent and Permissions: informed consent, outlining what data will be shared, how it will be used, and who will have access to it.

Privacy and Security

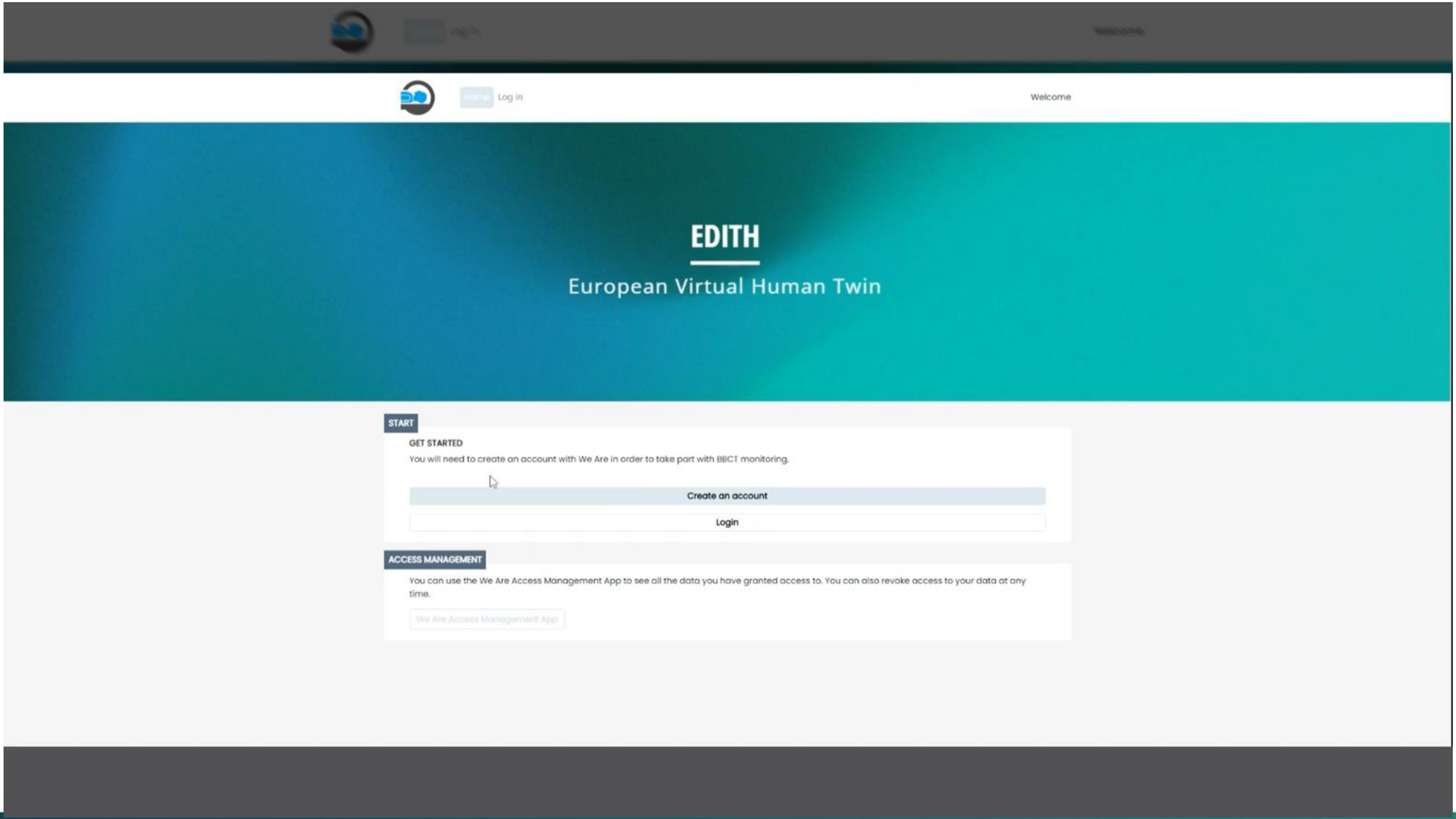
- *Only authorized personnel and the patient can view or use the data.*
- *Compliance with relevant data protection regulations*

Data Upload Methods:

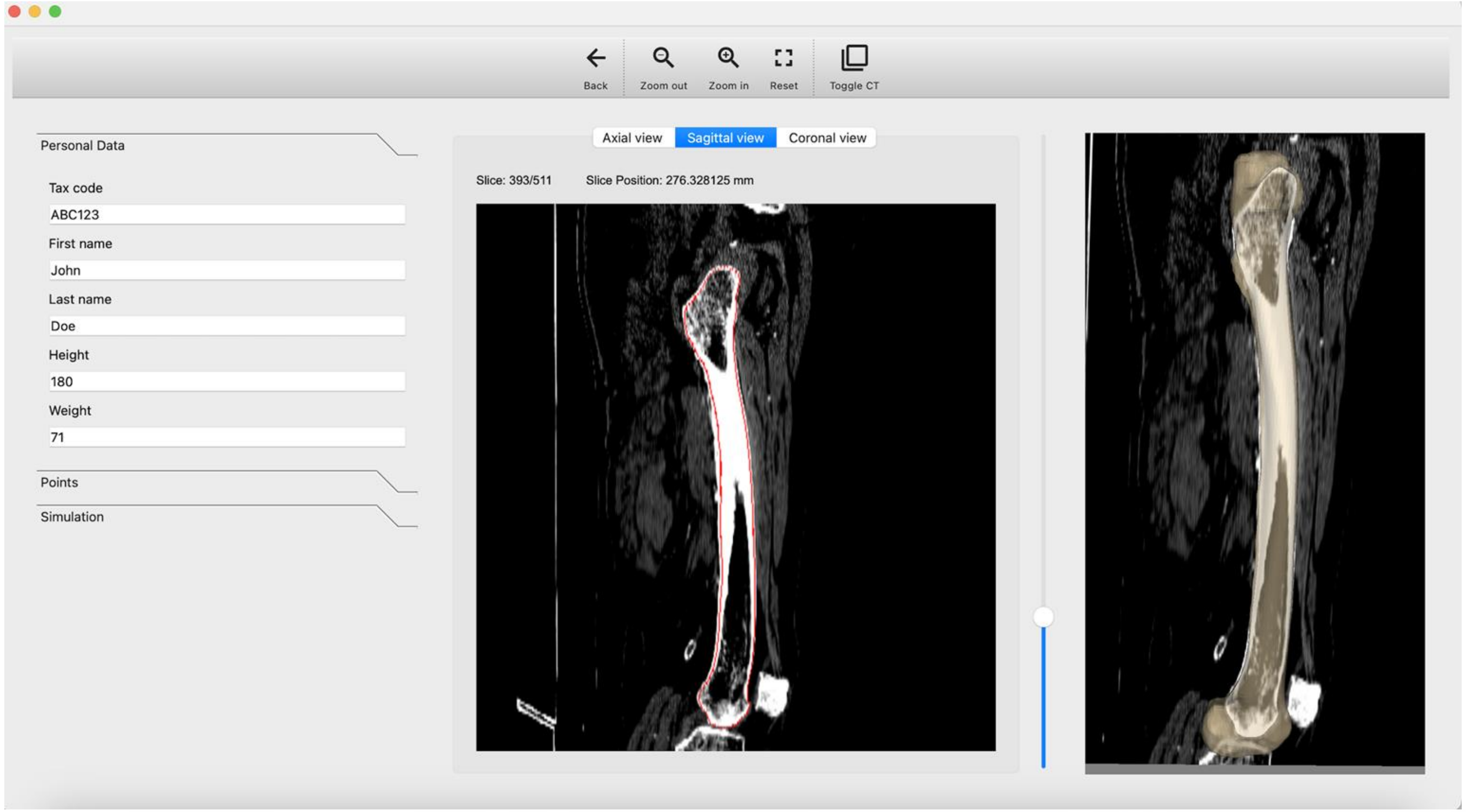
- Manual Entry: medical history, current medications, lifestyle information.
- Device Integration: Sync data from wearable devices
- Electronic Health Records (EHR) Integration: health records and lab results.

Different Data Types:

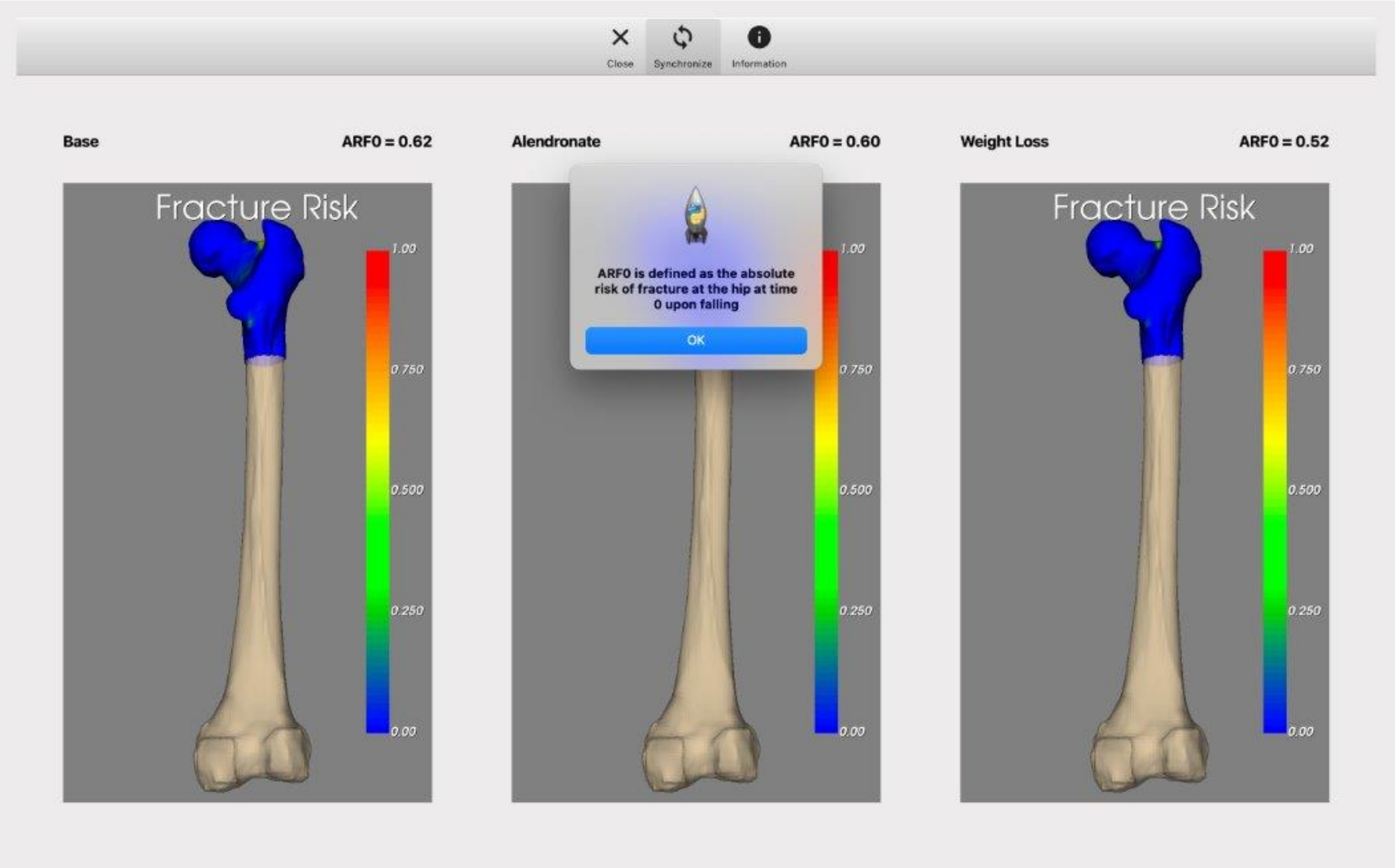
- Vital Signs, Biometric Data, Laboratory Results, Lifestyle Data, Symptom Tracking etc.


Log in
Welcome
EDITH
European Virtual Human Twin
START
GET STARTED
You will need to create an account with We Are in order to take part with BBCT monitoring.
Create an account
Login
ACCESS MANAGEMENT
You can use the We Are Access Management App to see all the data you have granted access to. You can also revoke access to your data at any time.

Use case: risk of fracture



Use case: risk of fracture



Benefits

Personalized Health Insights

- Tailored Recommendations
- Predictive Analytics

Personal Health Record Maintenance

Enhanced Disease Management

- Chronic Condition Monitoring (e.g., diabetes, hypertension, asthma)
- Medication Management (symptoms and side effects)

Improved Communication with Healthcare Providers

- Data Sharing
- Remote Consultation

User Friendly Visualisations and Statistics

Participate in Research

- Clinical Trials: Easily participate in clinical trials by providing relevant health data
- Crowdsourced Health Studies: Contribute anonymized data to larger health studies