Virtual Humans:
from Academy to Clinical Translation

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Who am I?

My (main) research topics (2000-2007)

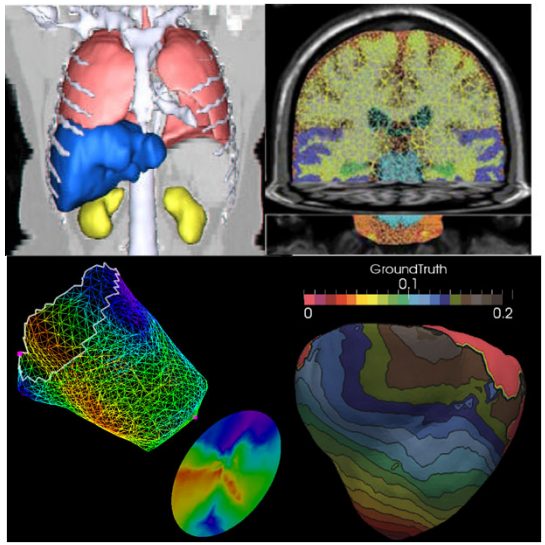
PhD (ENST Paris) on **image processing**, **oncology**

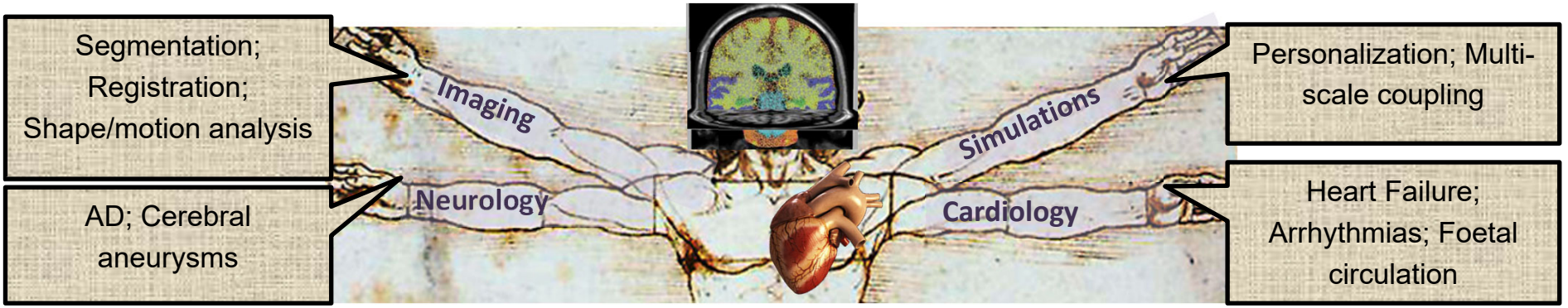
Postdoc (KCL, UCL) on **modelling** of **Alzheimer's Disease**

From 2007– until now

RyC, associate professor, **full professor** (UPF)

Cardiac data processing and **personalized modelling**

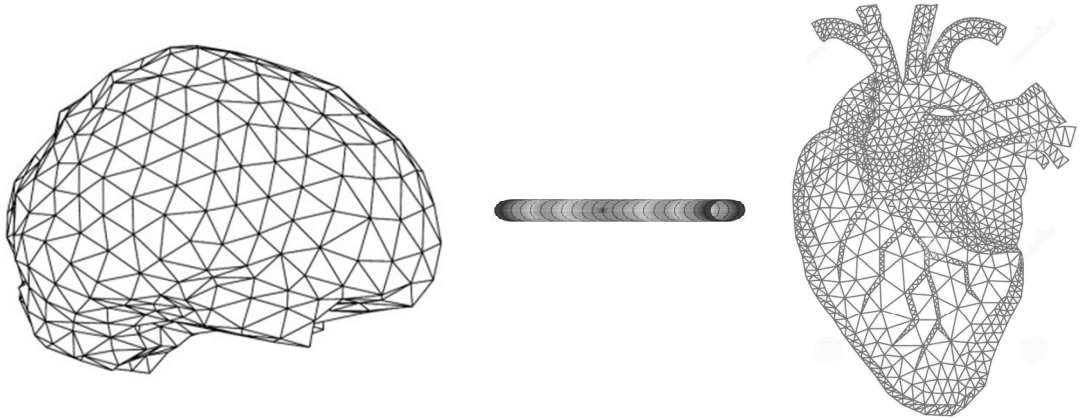




The Heart-Brain axis, or There and Back again: the journey towards brain development traverses vascular territories (Heart@Brain)

Brainstorming for applying to **ERC Consolidator grant**, 2015

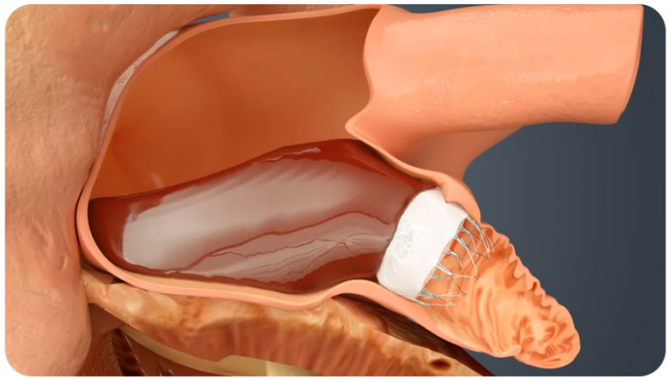
- 15 years working on computational tools in **neuro** and **cardio** → link the **Brain** and the **Heart** in a systemic/holistic approach



- 1st idea, for oldies: relation between **stroke** and **Atrial Fibrillation** (AF)

- 2nd idea, youngsters: influence of **cardiovascular abnormalities** in **brain development**

Left atrial appendage occluder (LAAO) devices

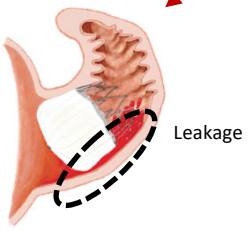


Boston Scientific Europe Left Atrial Appendage Closure with the WATCHMAN Device. https://www.youtube.com/watch?v=k-RzMGs0-pc

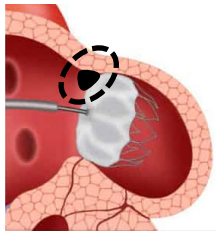
- **Alternative** for non-valvular AF patients
- **Non-inferiority** respected to lifelong OACS
- Successful closure **criteria**
  - Compression ratio (>10%)
  - Minimal peri-device leakage (<5mm)

→ **Device size and type selection**

Post-LAAO procedure



Peri-device leaks



Device-related Thrombus

- **2-17%** of incidence depending on device type
- **Multifactorial** process
- **Preventive treatments**
  - Oral anticoagulants
  - **Pulmonary ridge coverage**

upf.

COMPILAAO (2016-2019)

Spanish national project, Retos I+D (Ref: DPI2015-71640-R)

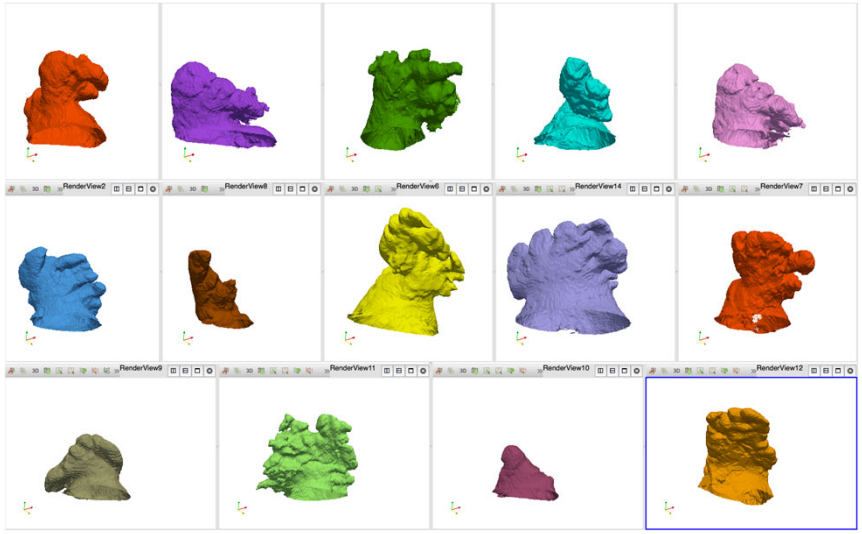
The main objective of the COMPILAOO project is to develop **advanced COMPutational tools** to characterize the **3D morphology of the LAA** and Investigate the **blood flow dynamics** and its relation to thrombus formation before and after **LAAO** interventions.

… as for cerebral aneurysms (same pipeline)

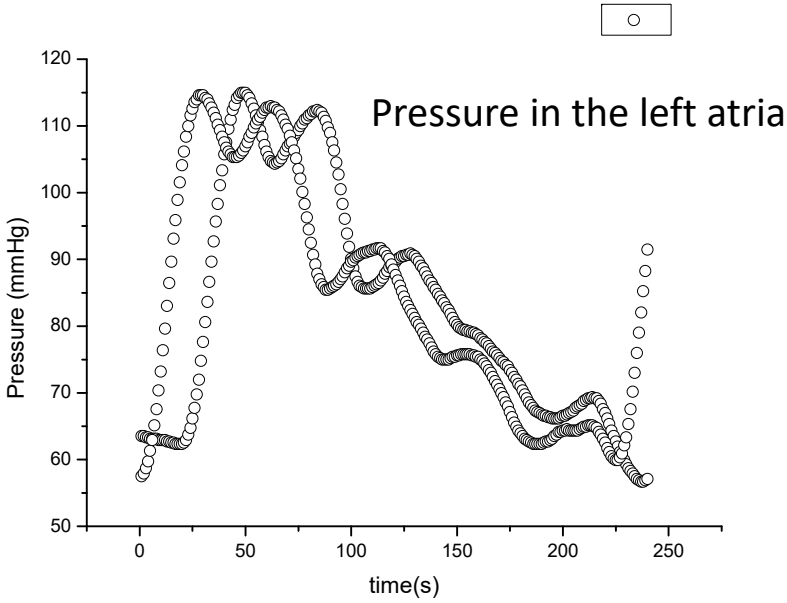
COMPILAOO data. 2017 status

Aalst

- Data from PVI and LAAO patients
- 37 LAA geometries from 3DRA (GE), already segmented
- 3 cases with echo data
- 1 pressure waveform for testing



Different LAA morphologies



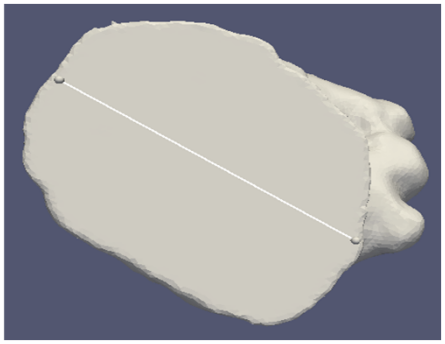
Hospital Clínic de Barcelona

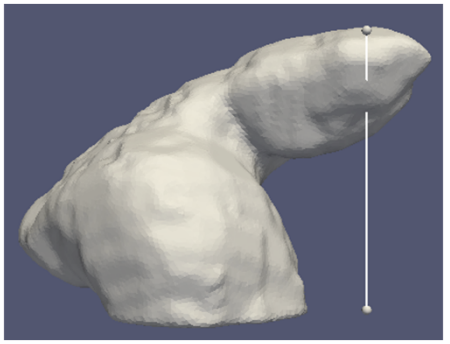
- Transfer of retrospective data to be started soon
- Possible involvement in a multi-centric clinical trial for anti-coagulants

Aalst data. Simple morphology characterization (2017)

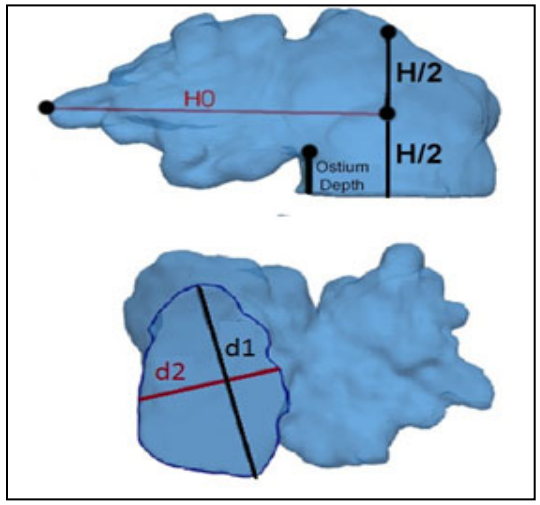
Simple measurements

- Orifice diameters
- Height

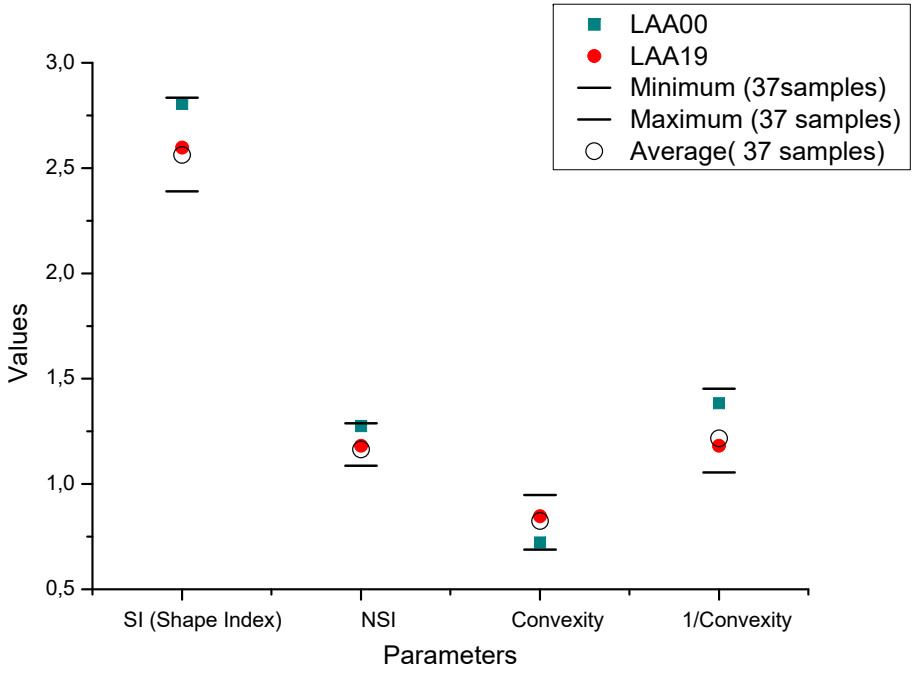




	Average diameter ostium (mm)	Average height (mm)
Cactus	24,20	27,31
Cauliflower	27,86	27,77
Chickenwing	26,53	22,64
Unknown	26,06	27,55
Windsock	28,64	32,05

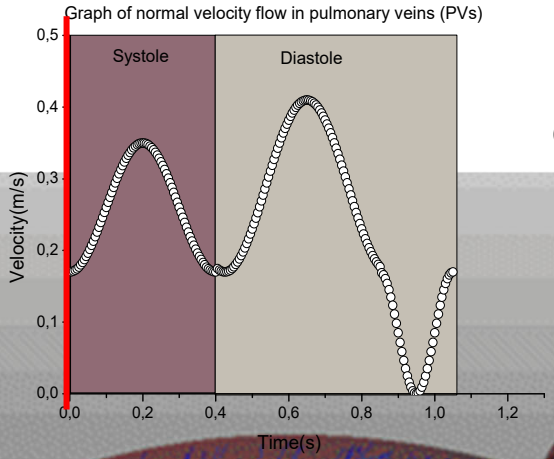


Fractal analysis (B. Paun)



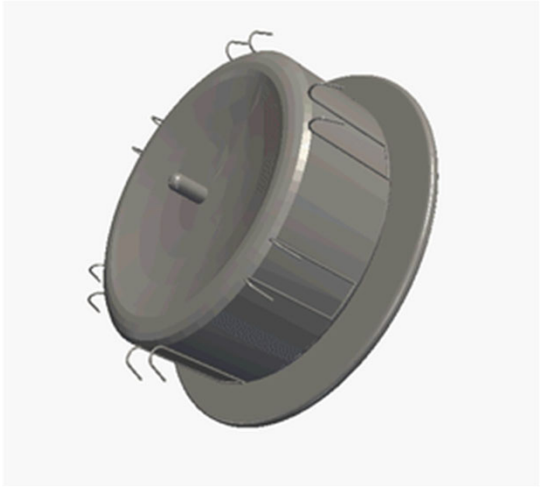
Aalst data. 1st fluid simulations – Synthetic atria (2017)

García-Isla et al., Int J Numer Method Biomed Eng 2018

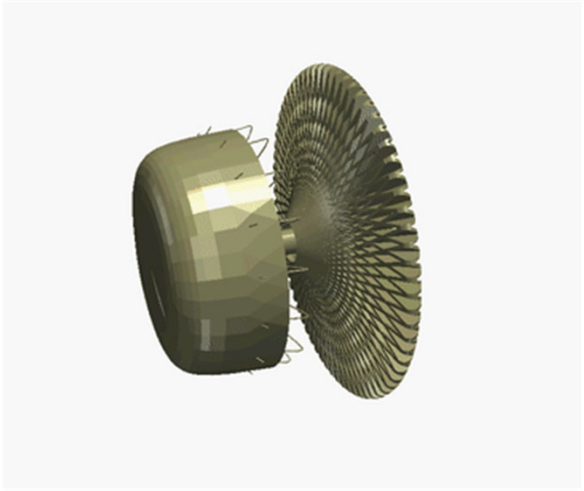


CAD models on LAAO devices (BSc students)

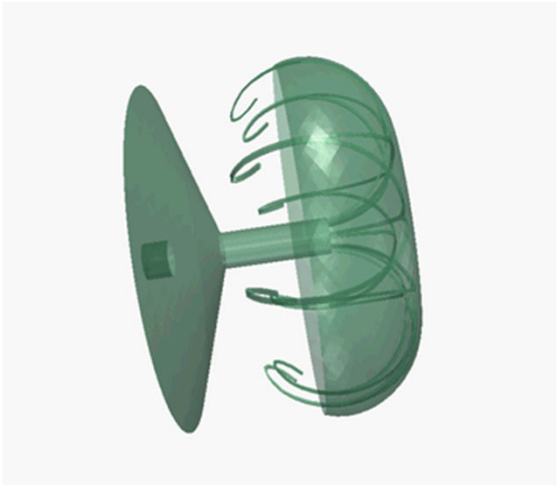
Amplatzer

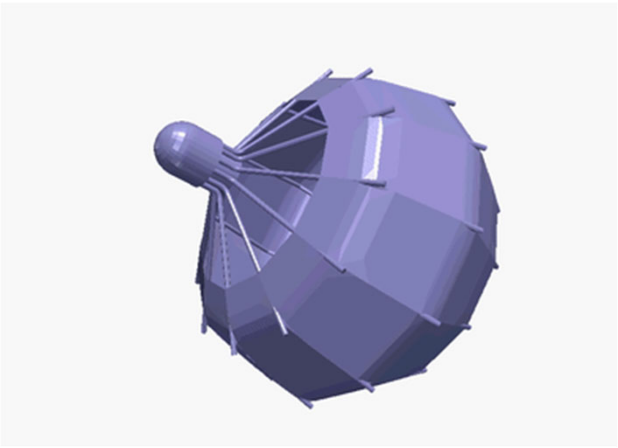


LAmbre



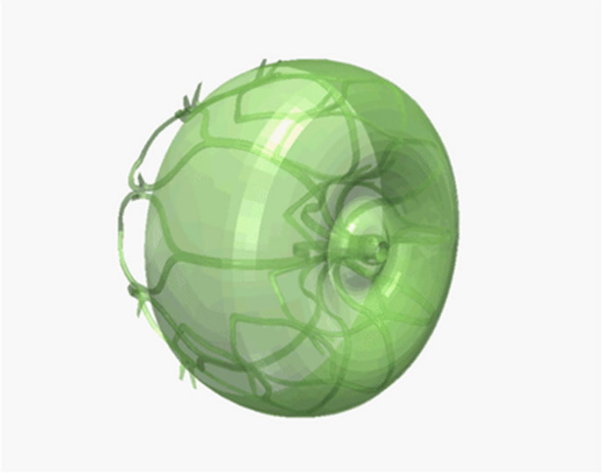
LAmbre





Platto

Watchman



Watchman

Continuous national funding over the years

COMPILAAO (2016-2019): Chicken wings in the heart?: **Comp**utational tools for **i**nvestigating the morphology and blood flow dynamics after **l**eft **a**trial **a**ppendage **o**cclusion interventions in atrial fibrillation patients

The main objective of the COMPILAOO project is to develop **advanced COMPutational tools** to characterize the **3D morphology of the LAA** and Investigate the **blood flow dynamics** and its relation to thrombus formation before and after **LAAO** interventions.

VIROLAAI (2019-2022): **VI**rtual/Augmented **R**eality and interactive tools for the in silico design, planning and follow-up **O**f **L**eft **A**trial **A**ppendage occlusion **I**nterventions

The main goal of the VIROLAAI project is to develop and **validate interactive tools** for the **training,** in silico **planning** and follow-up of LAAO interventions using a combination of **virtual/augmented reality**, multi-physics **simulations** and **advanced learning** technologies

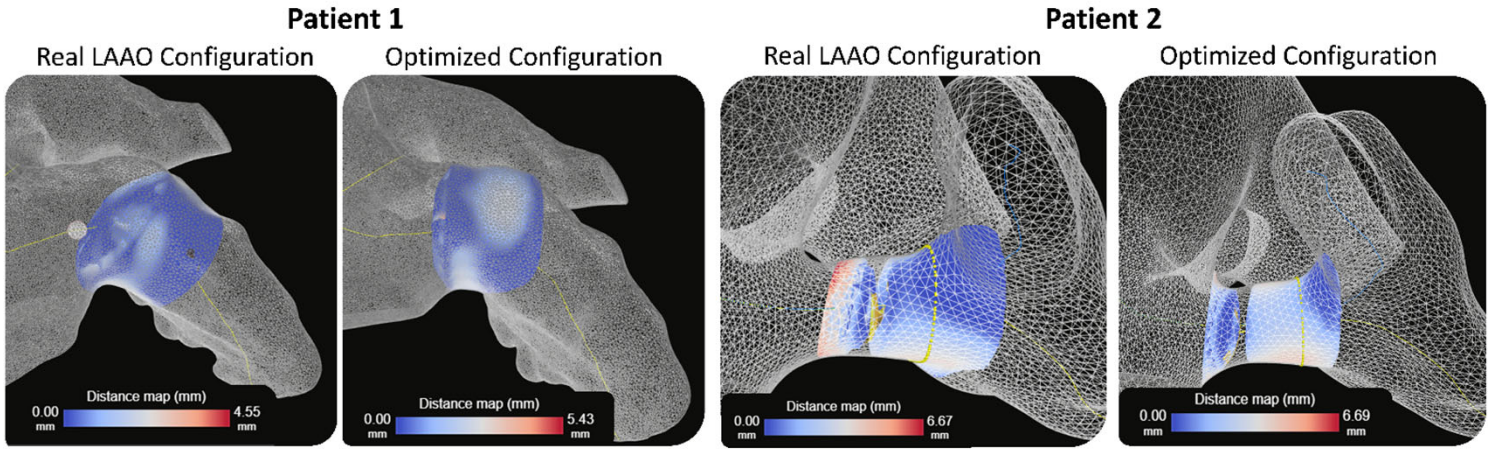
ATRAPAALO (2022-2024): **A**ccelerating technology **tra**nsfer and exploitation of computational tools for the **pla**nning of **l**eft atrial appendage occluder device implantations

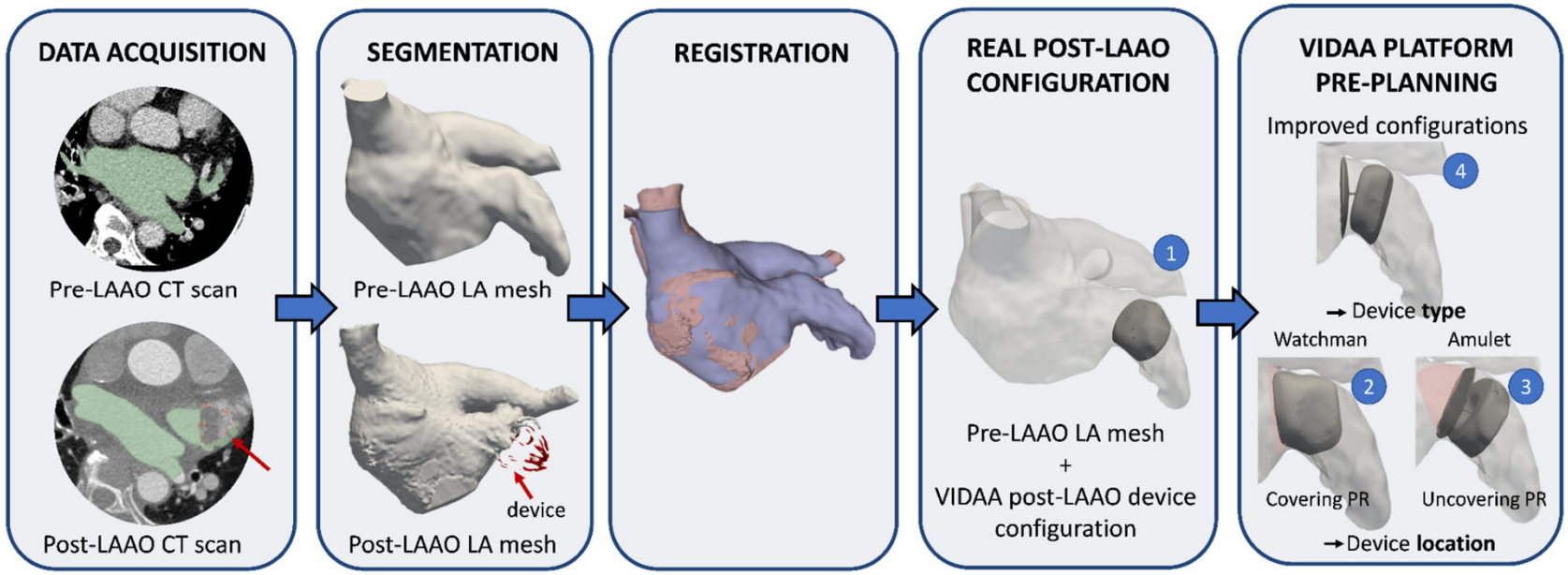
The main objective of the ATRAPAALO project is to **accelerate** the **transfer** and **exploitation** of computational technologies for the **planning of left atrial appendage occluder interventions**, based on the VIDAA platform and in-silico simulations.

GENERALITAAT (2023-2026): **Genera**ting synthetic data, knowledge, and c**li**nical recommendations with ar**t**ificial intelligence to improve left **a**trial **a**ppendage **t**herapies

The main goal of the GENERALITAAT project is to develop **advanced** computational techniques based on **artificial intelligence and biophysical models** to generate **synthetic data**, new knowledge, and **interpretable recommendations** to automatise and **democratise clinical decisions** related to left atrial appendage therapies

Fluid simulations with different device configurations

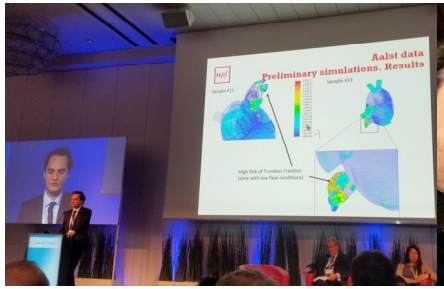




Albors et al., PLOS Comp Biol 2025

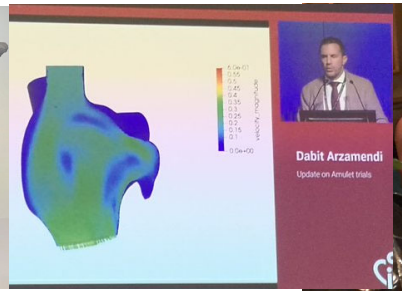
Presence over the years at CSI-LAAO, Frankfurt

CSI-LAAO'16

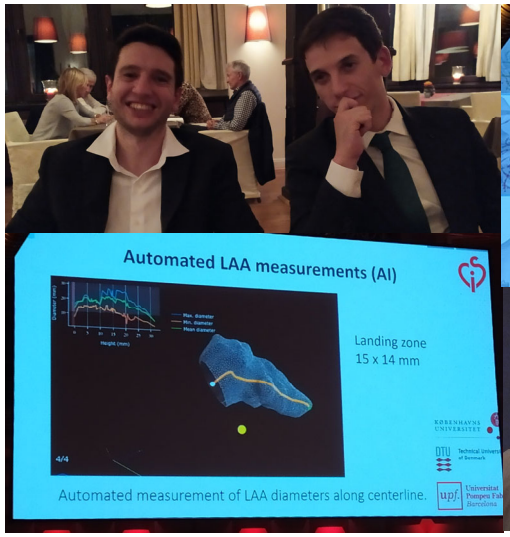


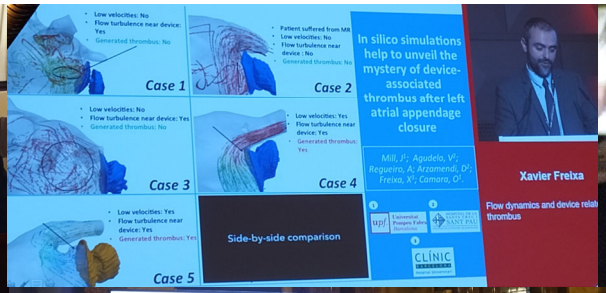
CSI-LAAO'17

CSI-LAAO'18

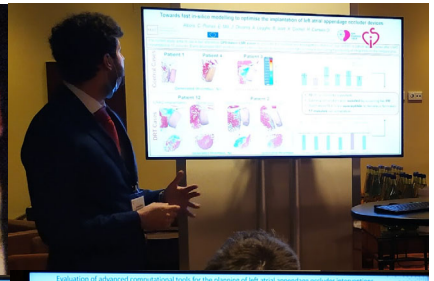


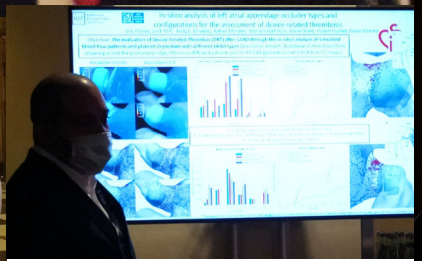
CSI-LAAO'19





CSI-LAAO'21

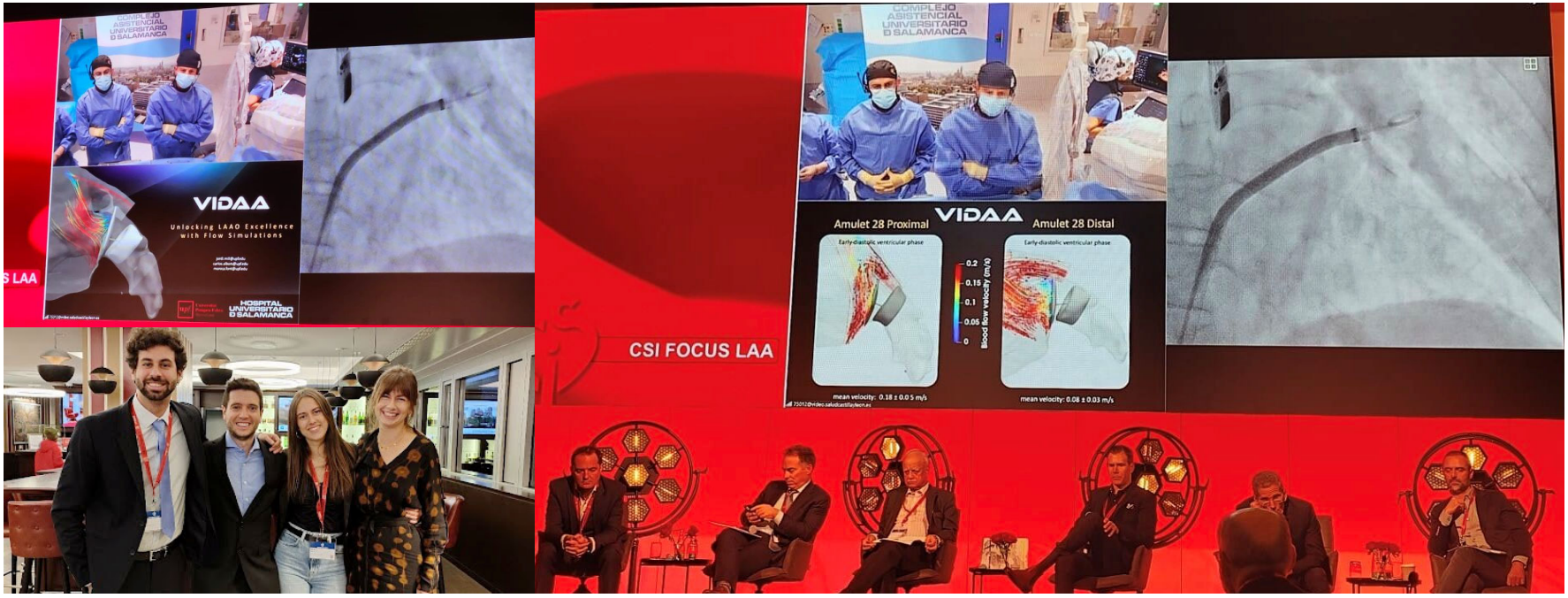




CSI & CSI-LAAO 2023, Frankfurt

CSI’23

CSI-LAAO’23



Need of user-friendly interfaces for clinical translation

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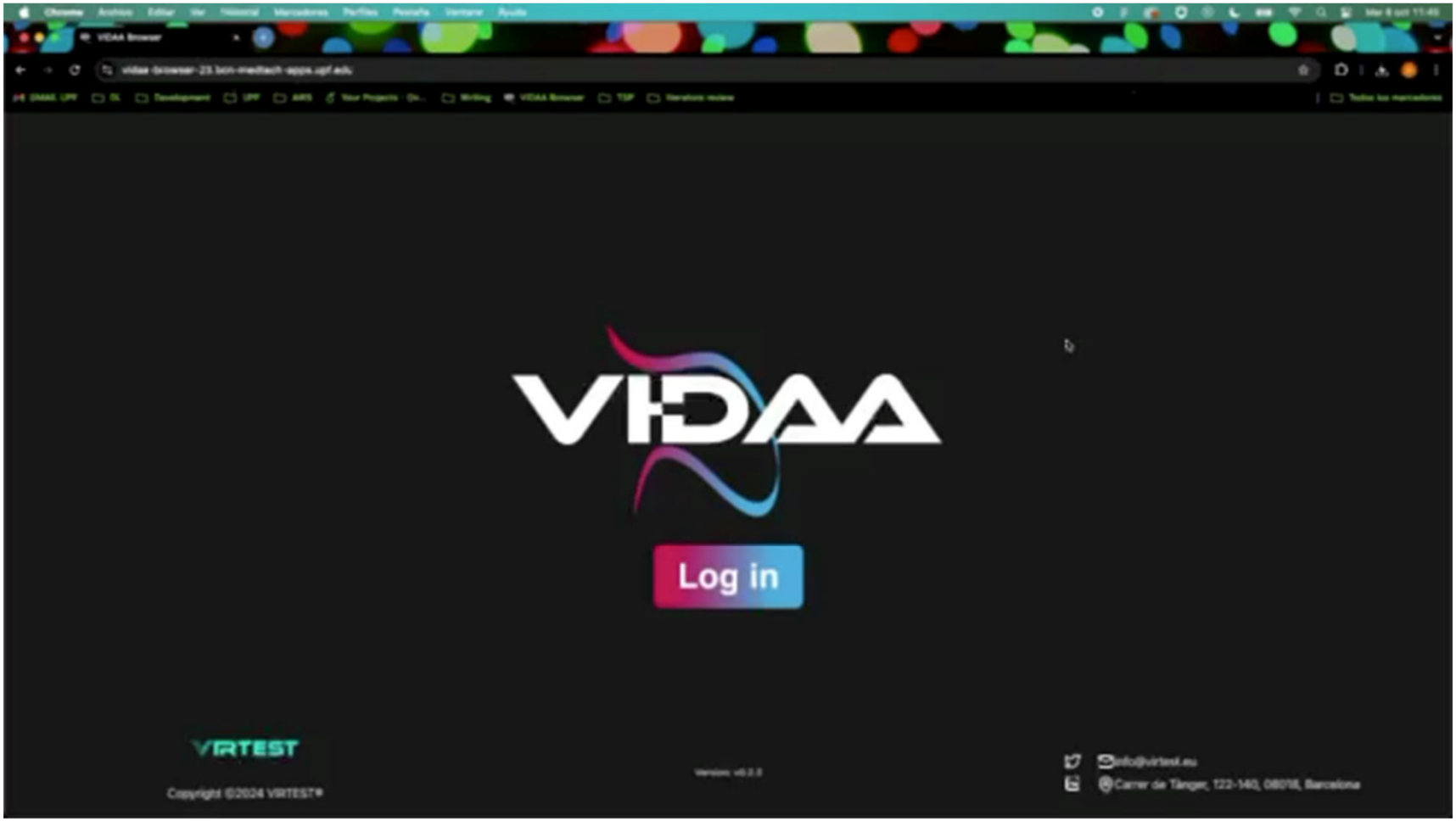
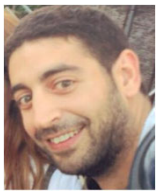
Pre-operative planning of left atrial appendage occluder implantations





Usual situation with our clinical collaborators

Missatge de Etel Silva <esilgar@gmail.com> del dia dj., 1 de juny 2023 a les 9:55:

> Hola!
> El lunes tenemos el cierre de otro paciente, este es el link con el CT y el VTK de la orejuela
>
> Si podéis subirlo a la plataforma para planificar un poco la intervención. Se lo quería enseñar hoy a un residente que es el que va a estar encargado de los análisis pre intervención con el VIDAA
>
> https://we.tl/t-K9wk8czePI
>
> Muchas gracias!
> Etel

(Free) Translation: Can you process this new case with your cool stuff, please? I need it in 2 days. I want to impress a new clinical fellow and "convince" (e.g., force) him to process the next 200 cases with your platform. And he needs a training session with you and help with doubts.

NON-SUSTAINABLE IN AN ACADEMIC ENVIRONMENT

VirTest Technologies spin-off

Barcelona Deep Tech Summit 2023

Foundation and 1st round of investment (1M euros)

GROW Venture Partners

Mobile World Congress 2023-24

SimCardioTest project (2021-2024) → AI, Visual Analytics and Digital Twin

SimCardioTest will develop a **standardised and secure cloud-based platform** where **in-silico trials** run seamlessly. **Three cardiac use cases** will demonstrate the platform effectiveness, along with the required **verification & validation processes** and **certification support** of the medical device or medicine.

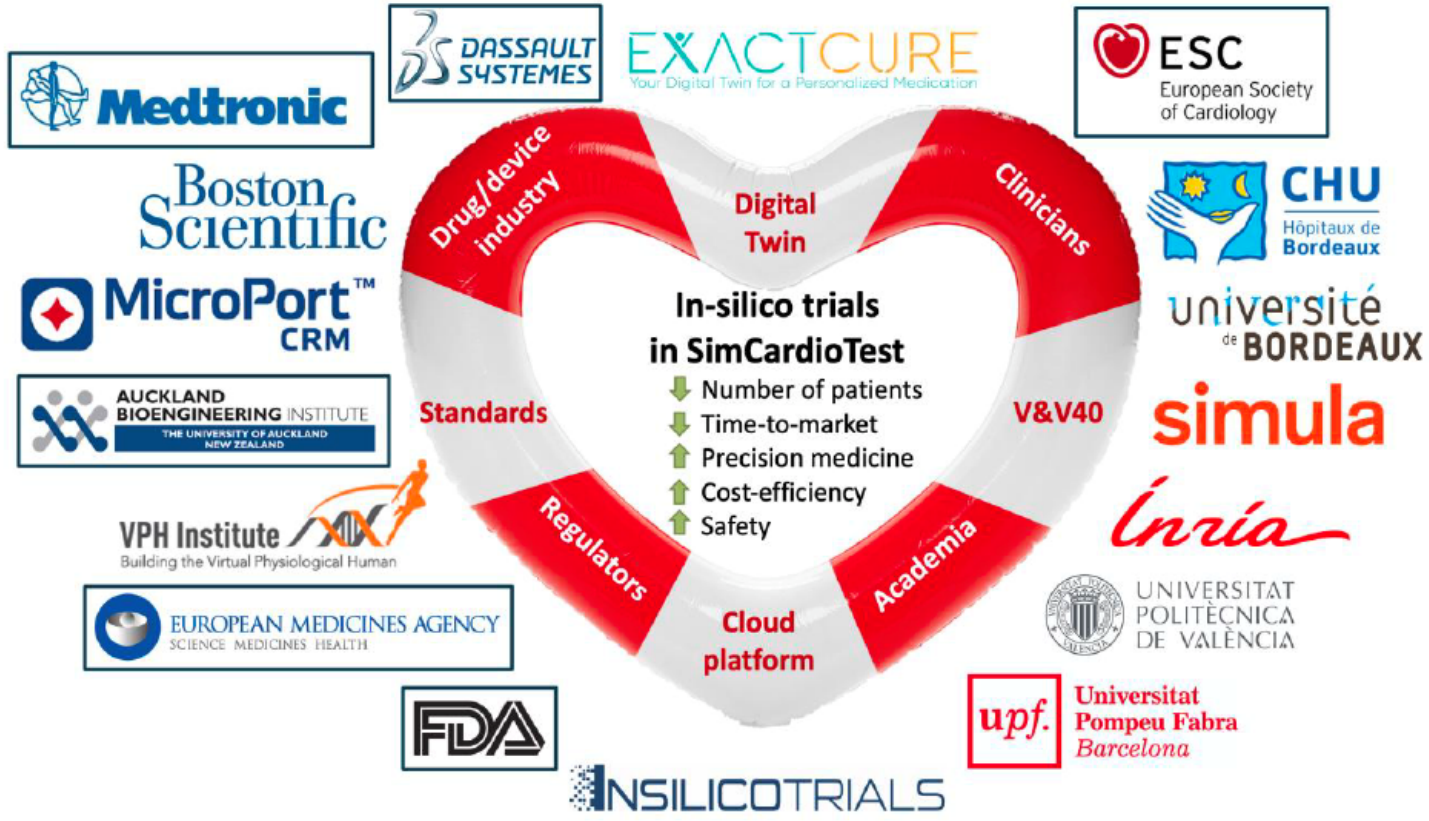
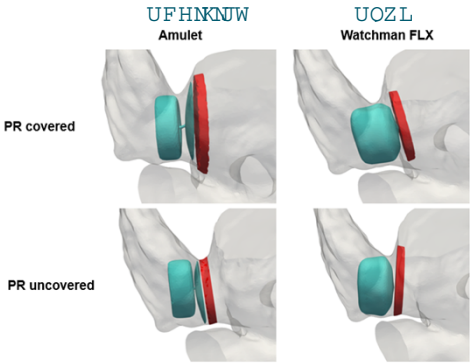
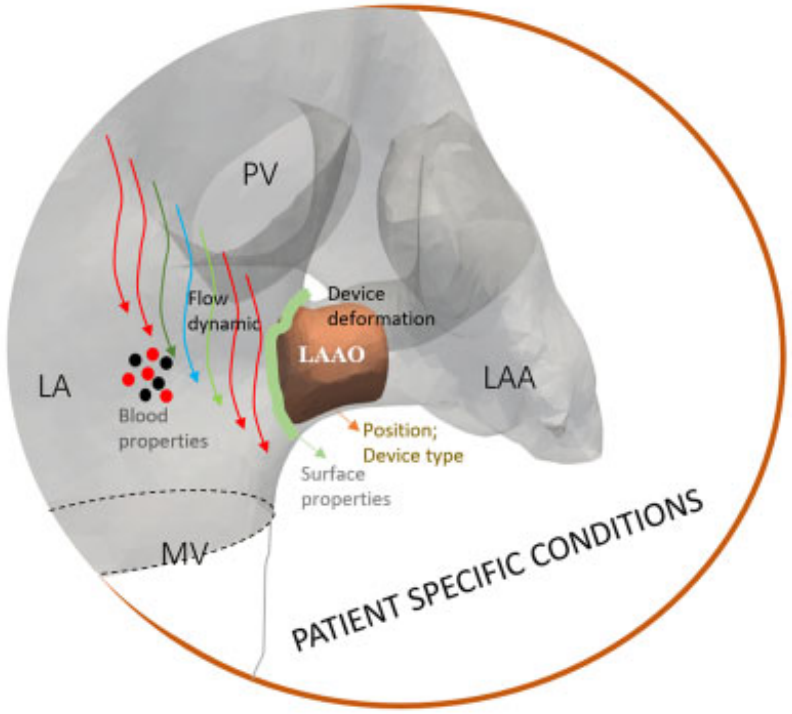


Figure 2: SimCardioTest in-silico trials: a life buoy for healthcare innovation in cardiovascular diseases. Blue frames: advisory board members.

V&V40 for LAAO devices

QoI: Does covering of the pulmonary ridge with a LAAO device (plug or pacifier) relates with the likelihood low blood flow velocities (e.g., < 0.2 m/s) around the device and inducing the device-related thrombus (DRT)?

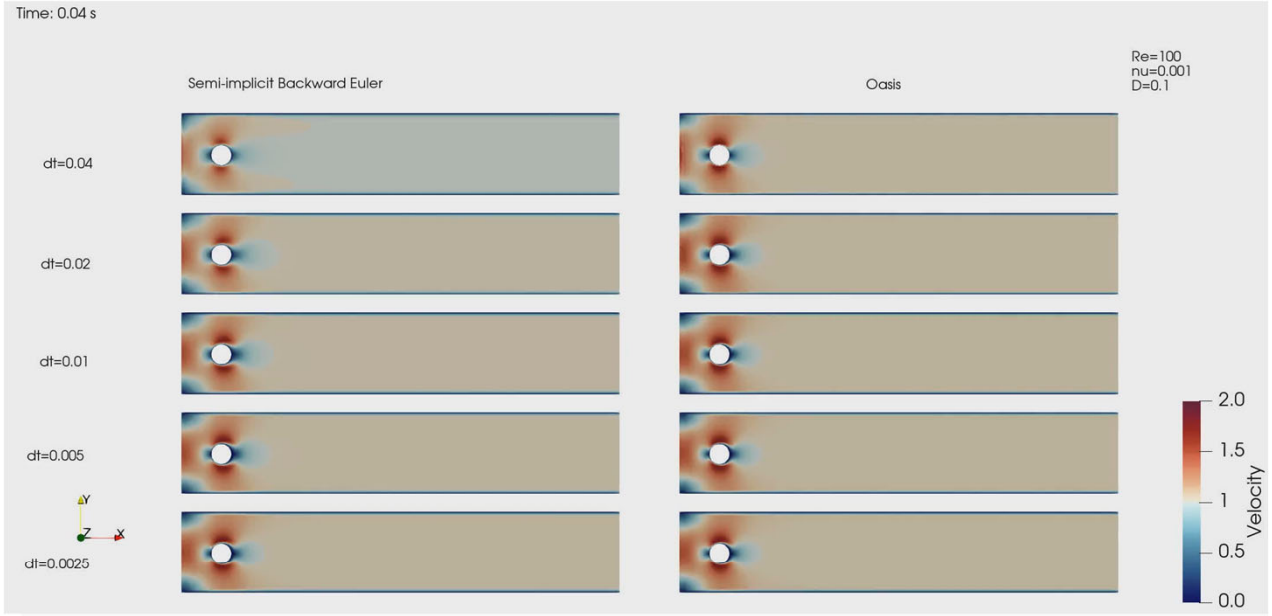




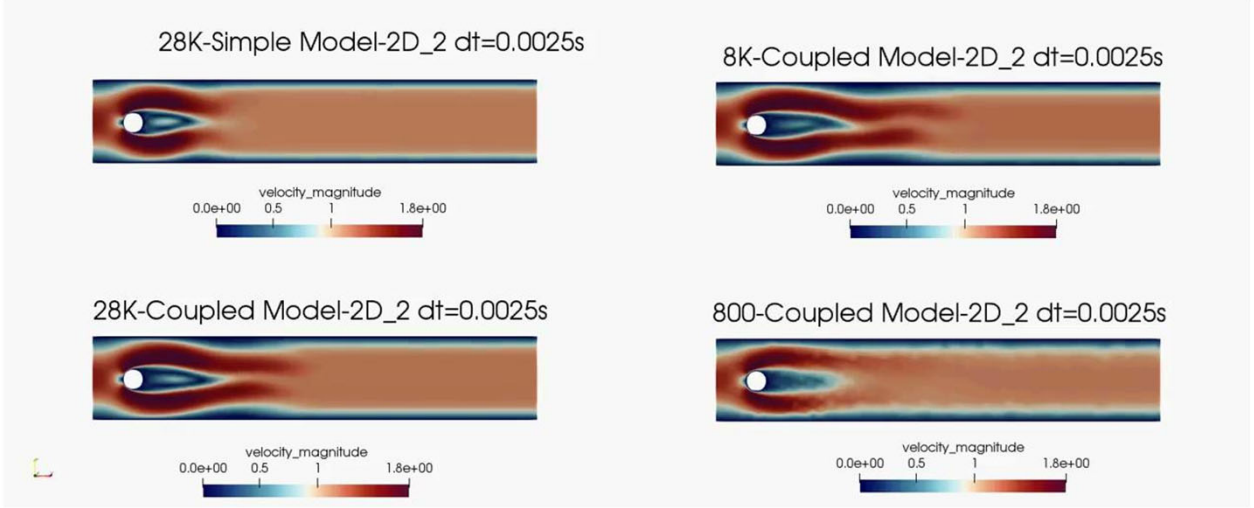
V&V40 for LAAO devices – spatial/time convergence studies

simula

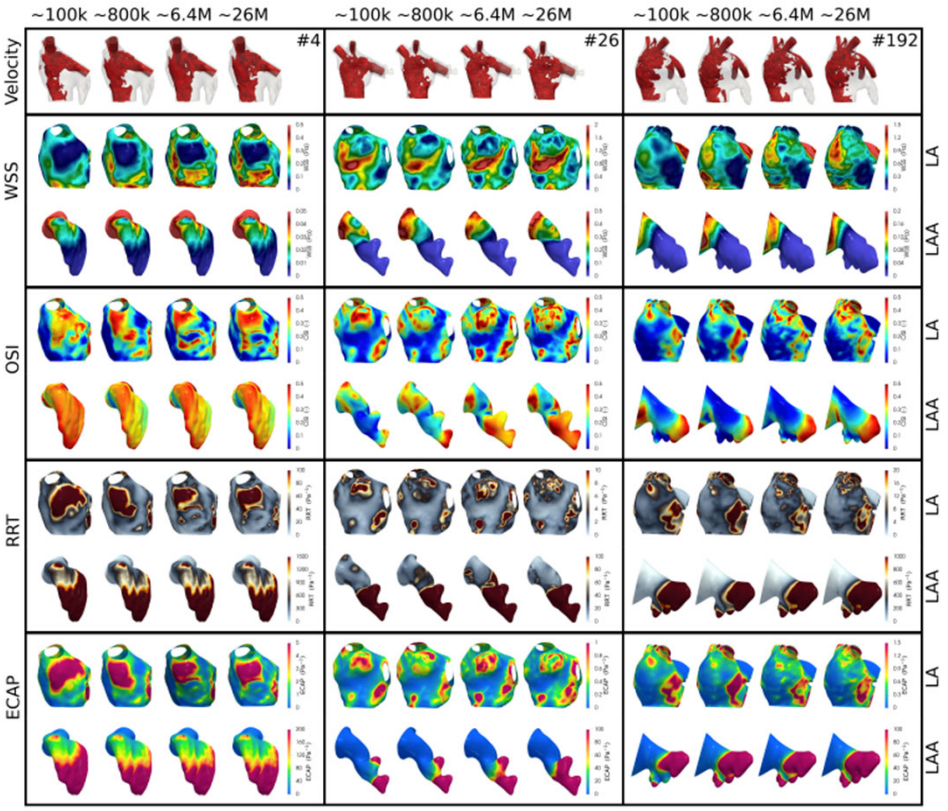
Comparison of Ansys-like and Oasis solvers with different time-steps



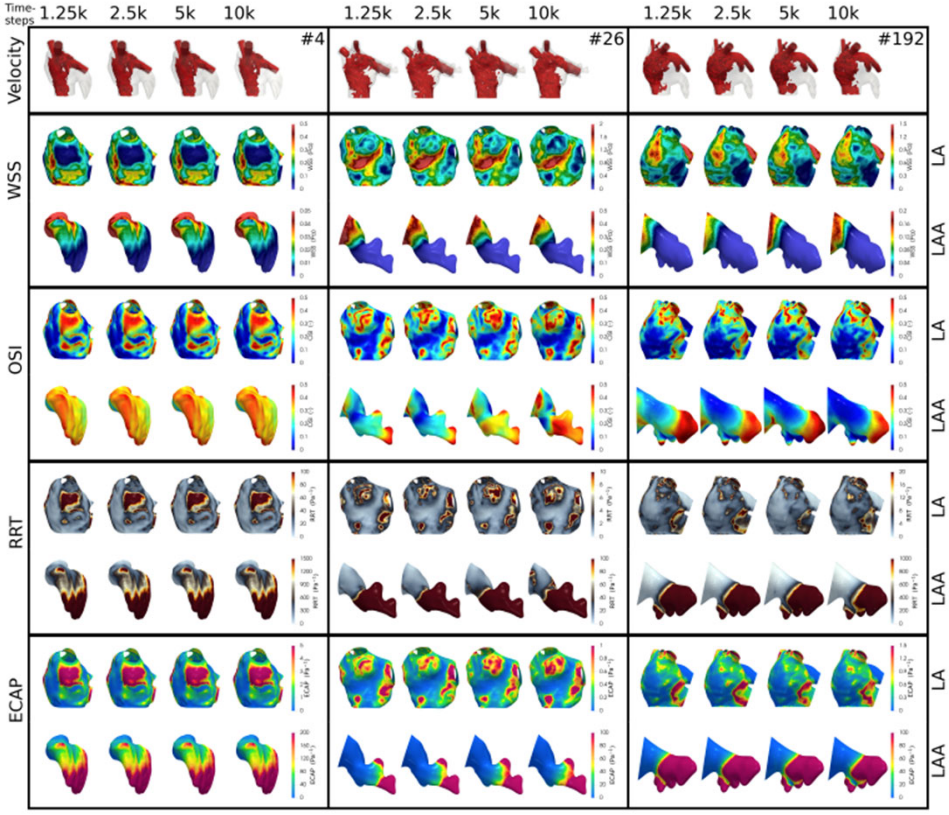
Ansys results with different spatial resolutions and models



V&V40 for LAAO devices – Convergence tests with clinical data



Mesh convergence



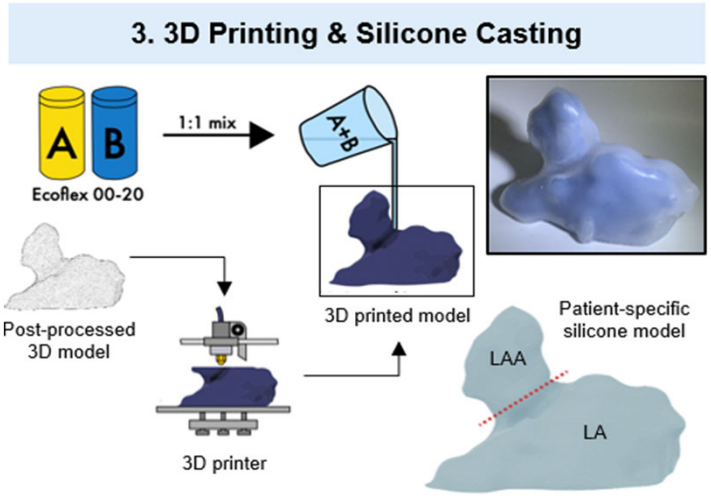
Time-step convergence

Khalili et al., Int J Numer Method Biomed Eng 2024

Validation with in-vitro phantoms

SEGMENTATION → 3D Printing → MOCKUP

UPF PROTOCOLS	MIT PROTOCOLS	MIT PROTOCOLS
- CT images - Source CT system - Isotropic voxel sizes (e.g., ranged between 0.37-0.5 mm; 512 x 512 x [270-403] slices - Using region growing and thresholding in 3D-slicer software -Taubin smoothing	- Object Connex 500 - Silicone casting (Ecoflex00-20) - Pneumatic artificial muscles (PAMs)	-Pressure measured in the LA/LAA - Flow inlet was controlled -Flow velocities can be measured with US or PVI



Massachusetts Institute of Technology
Harvard–MIT Health Sciences & Technology
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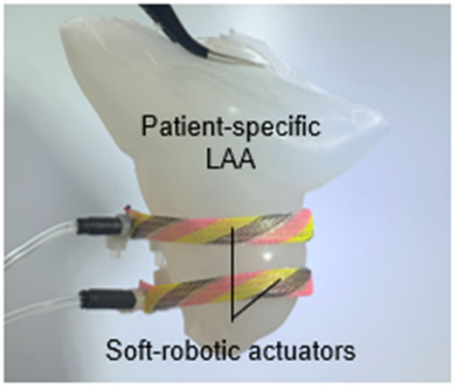
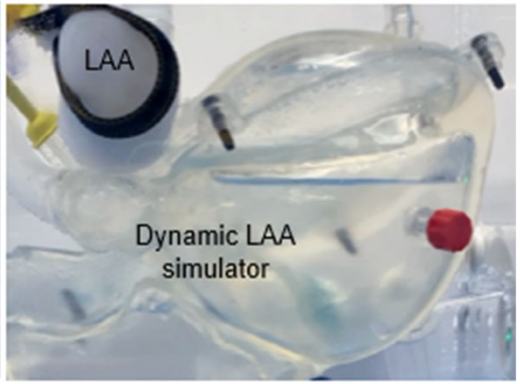
MITMECHE

4. Insertion into Dynamic Simulator



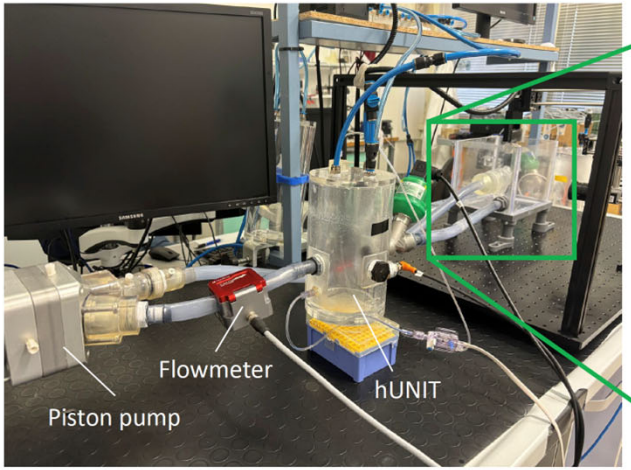


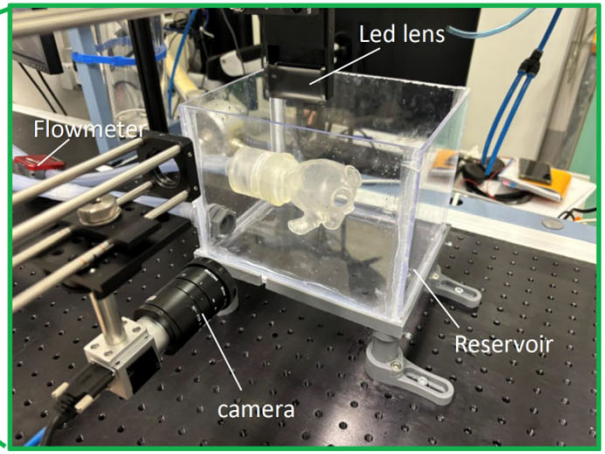
Roche et al., Nat Biomed Eng (to appear)

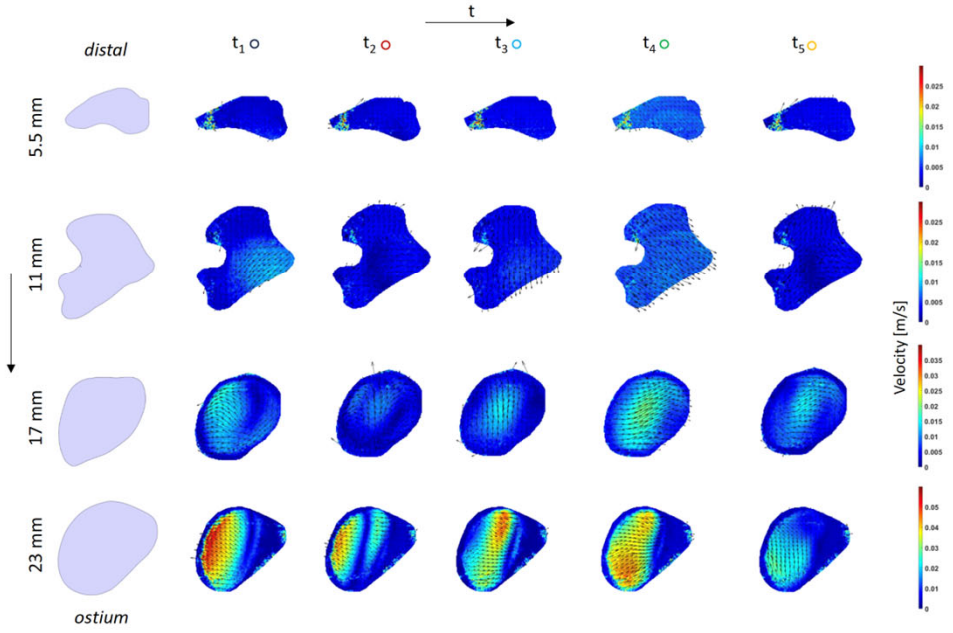
Validation with in-vitro phantoms

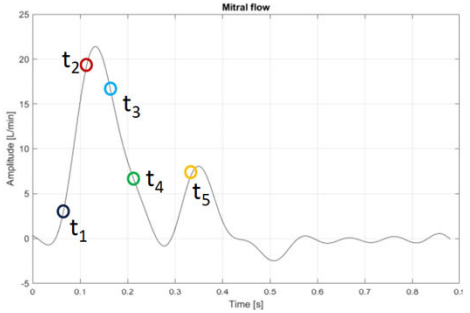
Gasparotti et al.,

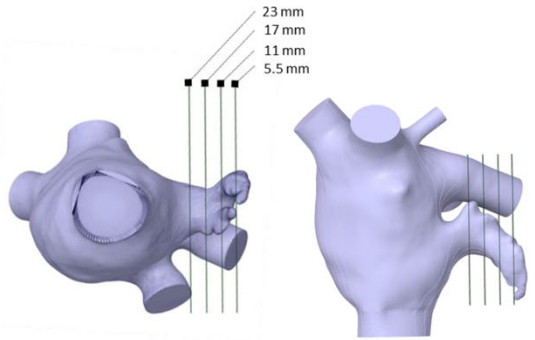
FIMH25











Data for the FLAMES workshop

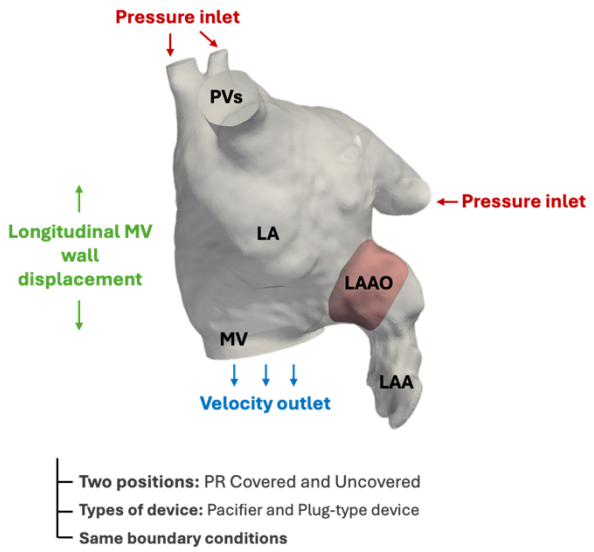
Gasparotti et al., FIMH'25

Large uncertainty quantification studies

Working directly with Ansys to optimize whole modelling pipeline

Automatization of segmentation, mesh generation, and boundary conditions

Having dedicated people for years …



AF, Newtonian

AF, non-Newtonian

No-AF (Add MV A-wave), Newtonian

AF (MV velocity x1.25), Newtonian

AF (MV velocity x0.75), Newtonian

AF, Newtonian, Rigid walls

AF (PVs pressure +1.5 mmHg), Newtonian

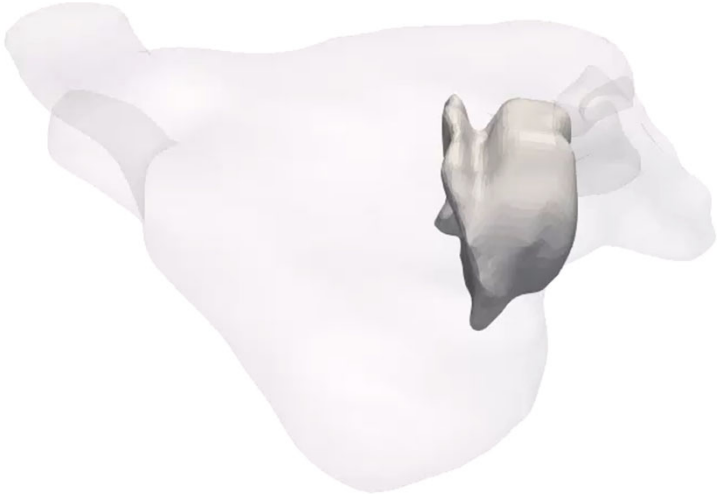
› > 1400 simulations

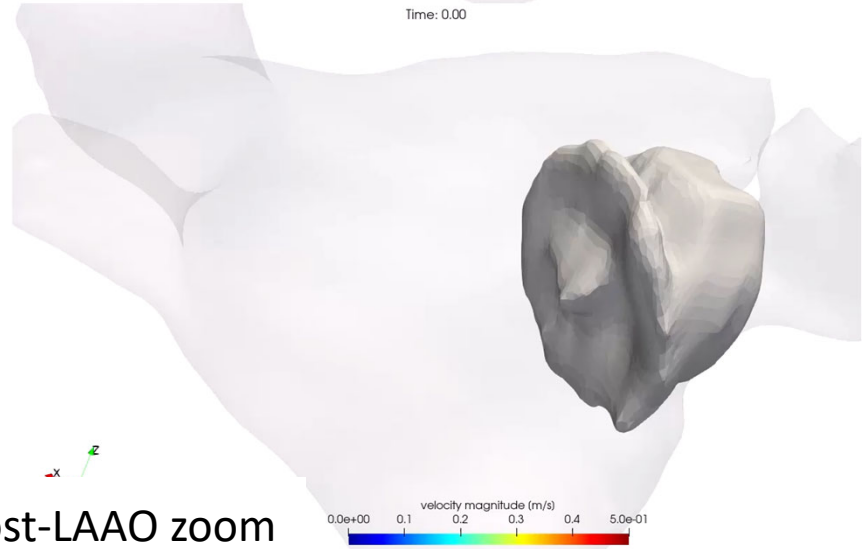
Barrouhou et al., CMBBE'25

4D flow MRI with LAAO devices

Pre-LAAO

Post-LAAO

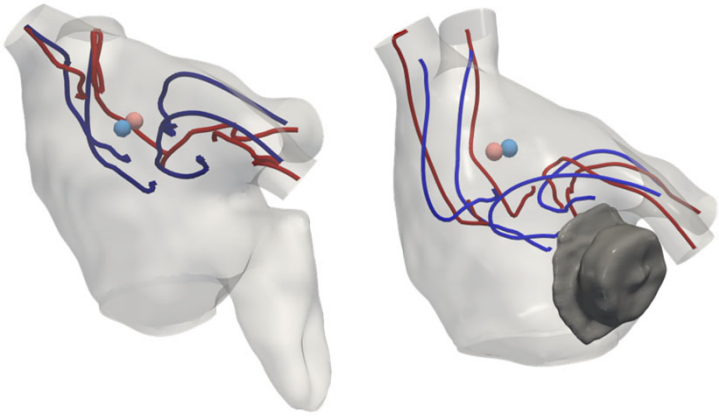




Post-LAAO zoom
Leak is present

Pre-LAAO

Post-LAAO



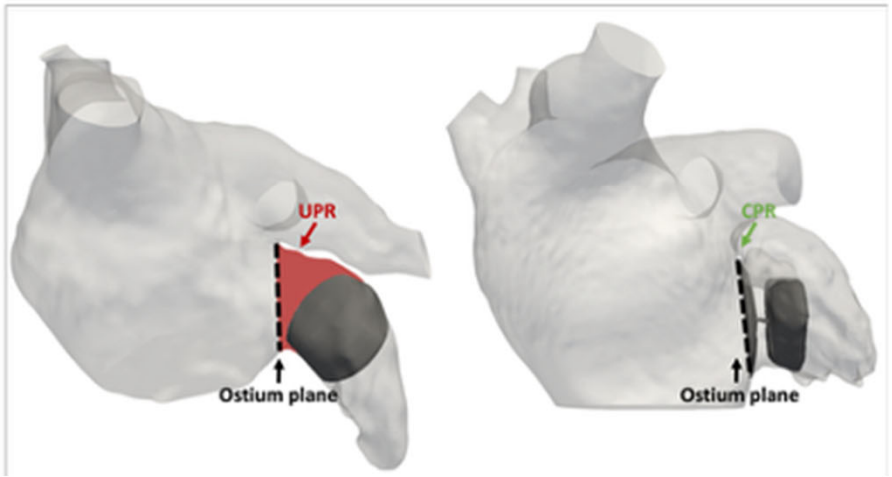
Red: CFD; Blue: 4D flow MRI

Morales et al., JACC Intv'24; Casademunt et al., STACOM'24, WSC'25

IDEAL study – retrospective in-silico clinical trial on LAAO position

Primary outcome

- Differences in flow dynamics between device position and device type in relation to device-related thrombus.

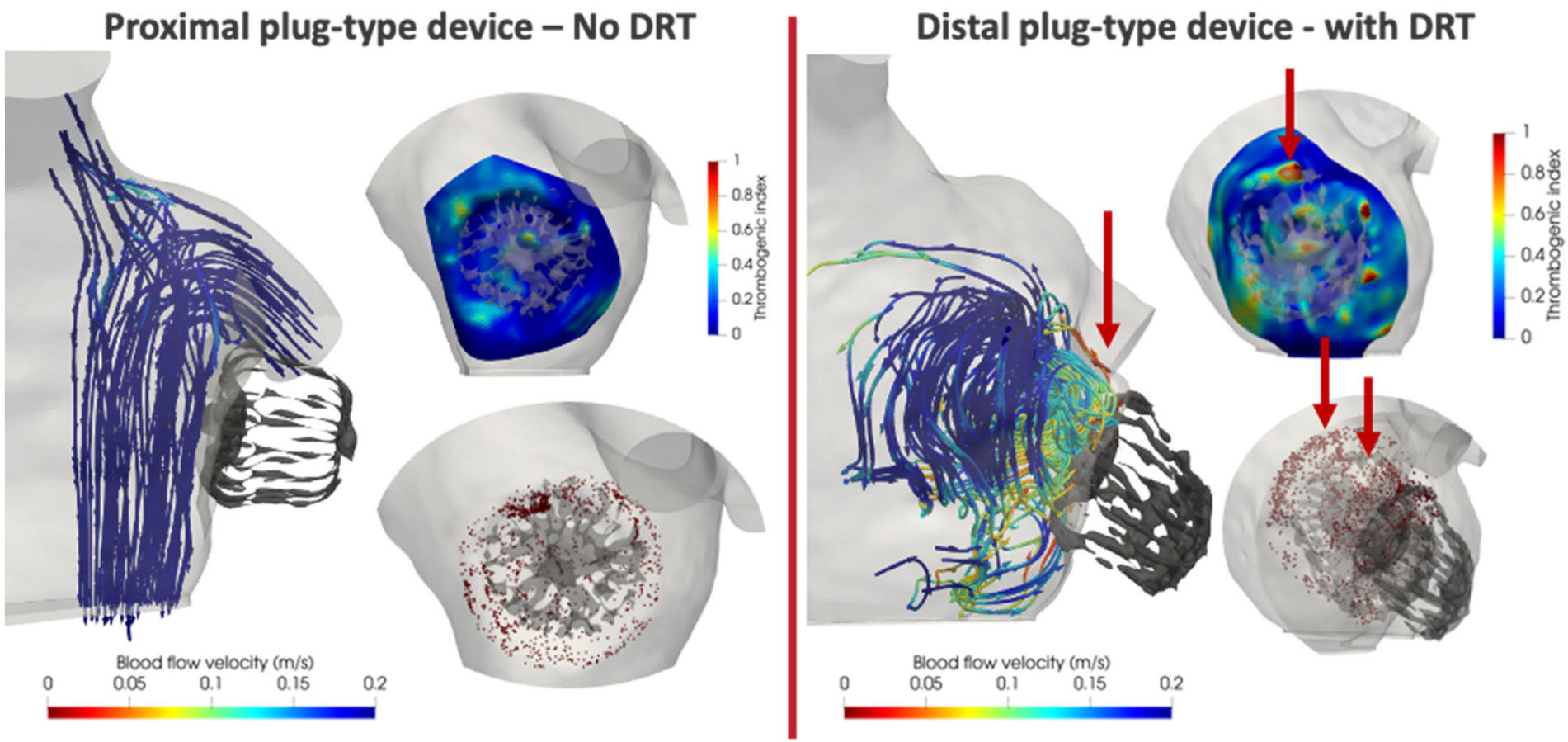


292 cases have been simulated and analysed. Main challenges?

- Getting the data from all hospitals in a secure and accepted way
- Analysing and visualising that big amount of simulations

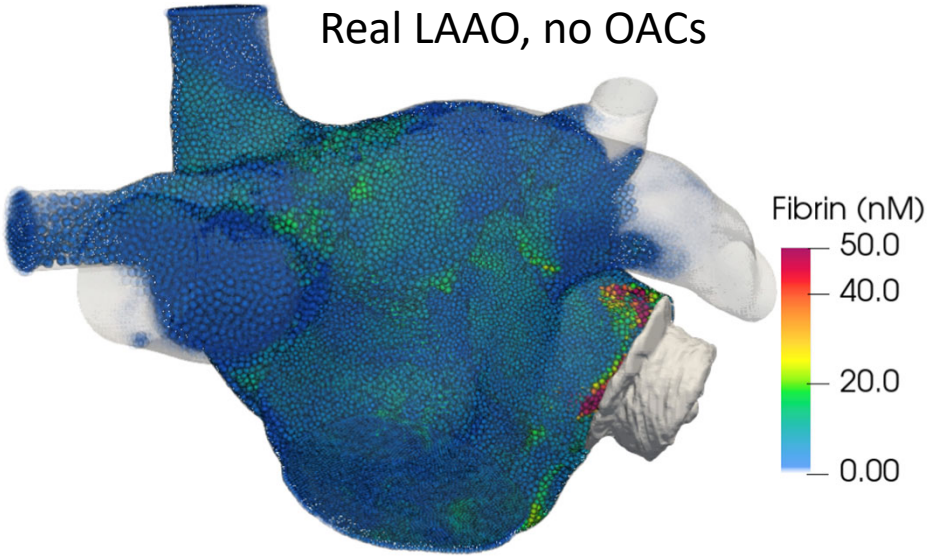
Cepas et al., submitted

In-silico clinical trial on LAAO position

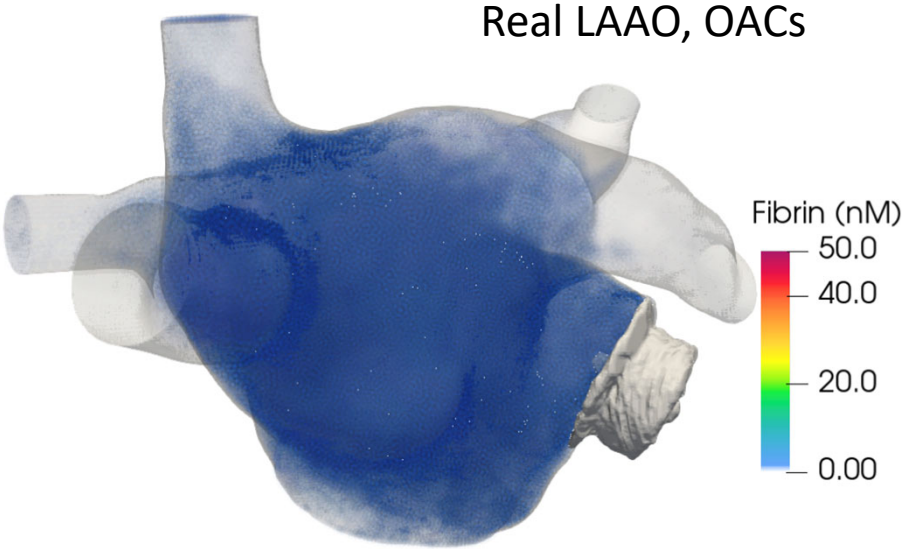


Drug-device interaction → anticoagulants + LAAO

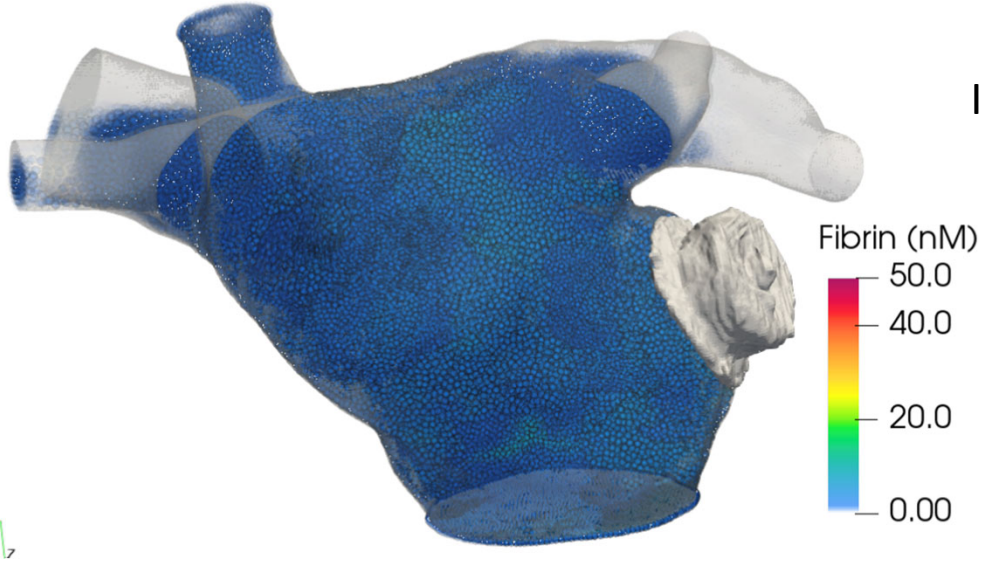
Real LAAO, no OACs



Real LAAO, OACs

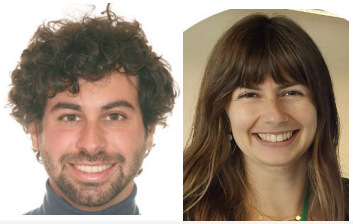


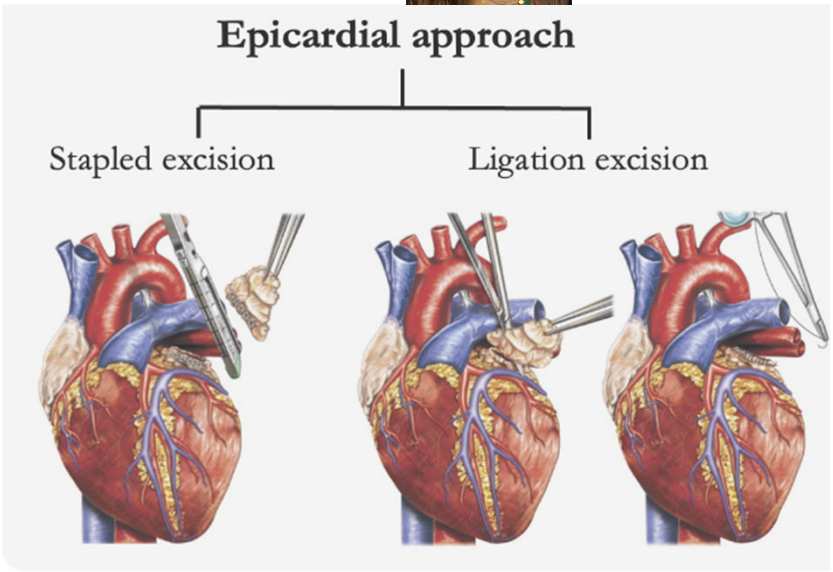
Ideal LAAO, no OACs



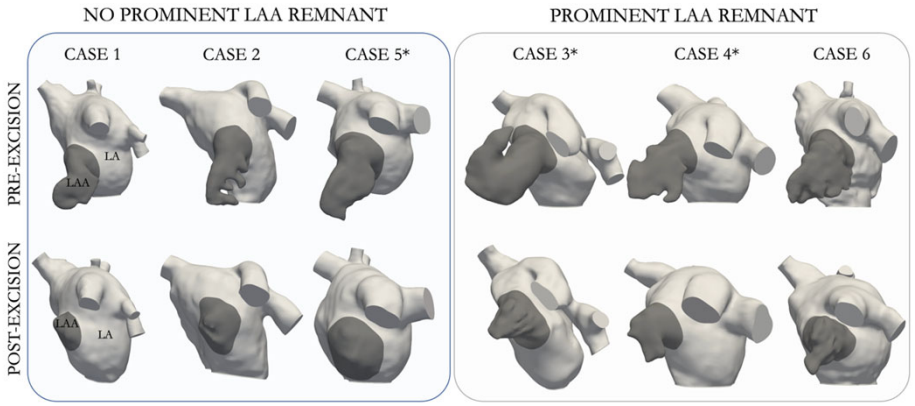
Segarra et al.,
JACC Case Rep 2025

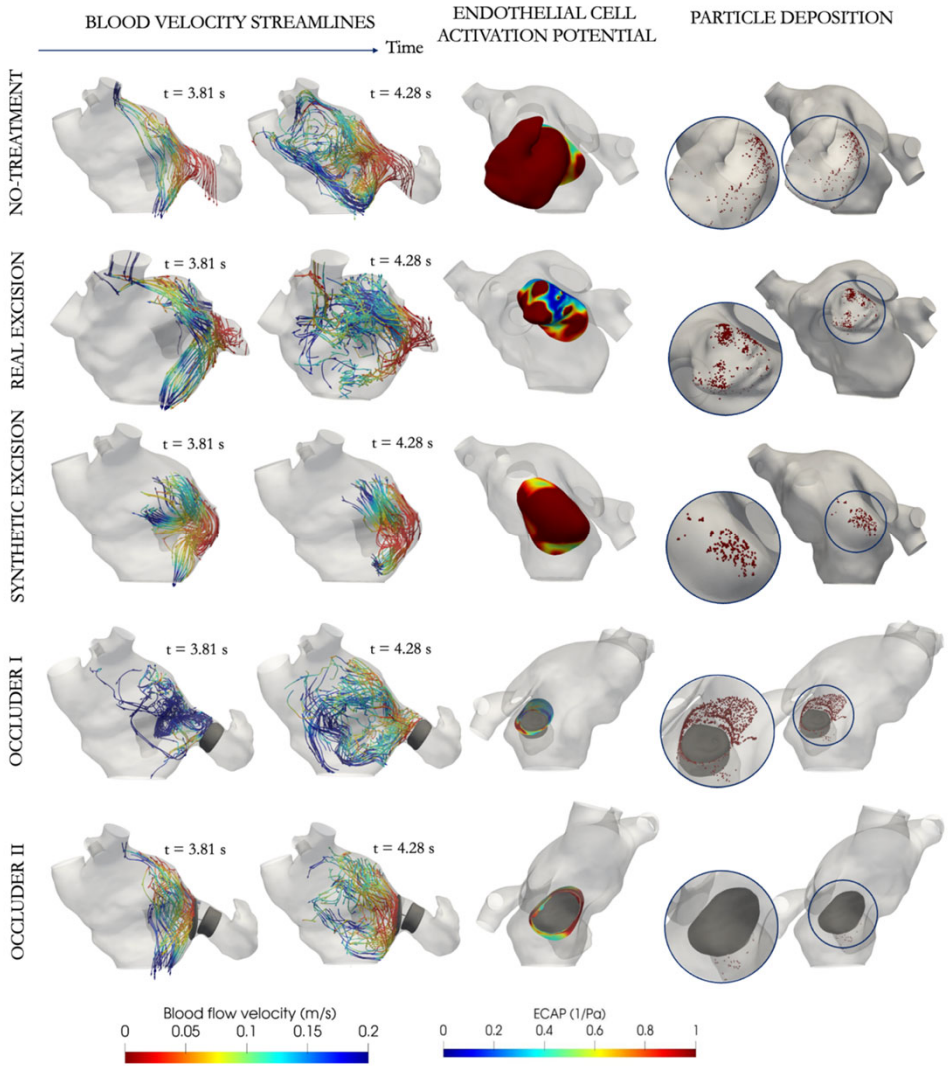
Fluid simulations for thrombus risk after LAA excision





D'Abramo et al., Rev Cardiovasc Med23

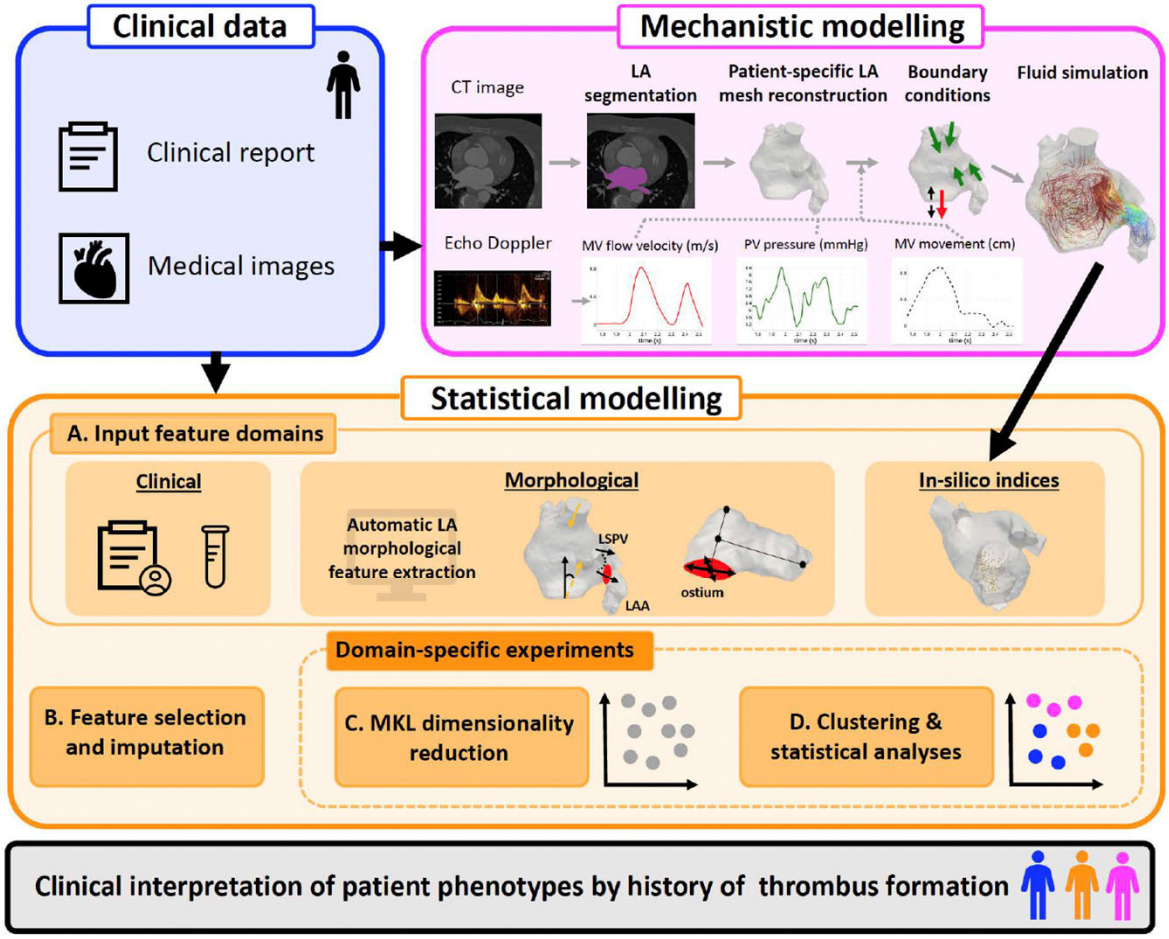


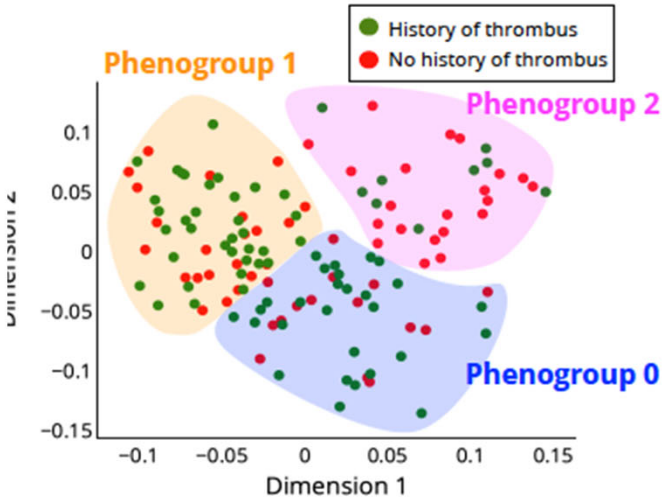


Albors et al., Comput Biol Med 2025

Then, possible to integrate digital twin with other multimodal data

Unsupervised machine learning for finding phenogruping patients based on stroke risk





Phenogroup 0
33% h/o thrombus
- ↓ ostium area
- ↓ LAA tortuosity
- ↓ non-CW LAA/LSPV alignment
- ↓ number of LAA particles
- 57% non-paroxysmal AF
- ↑ BNP
- ↑ creatinine
- ↑ ratio MPV/platelet count
- ↑ hematocrit

Phenogroup 1
40% h/o thrombus
- ↓ ostium area
- ↓ LA and LAA volume
- ↑ ratio ostium area / LAA vol.
- ↓ LAA centreline length
- ↓ LAA tortuosity
- ↓ non-CW LAA/LSPV alignment
- ↓ number of LAA particles
- 46% non-paroxysmal AF
- ↓ BNP
- ↑ LVEF
- ↓ creatinine
- ↓ ratio MPV/platelet count
- 35% female
- ↓ cardiac insufficiency

Phenogroup 2
70% h/o thrombus
- ↑ ostium area
- ↑ LA and LAA volume
- ↓ ratio ostium area / LAA vol.
- ↑ LAA centreline length
- ↑ LAA tortuosity
- ↑ LAA sphericity
- ↑ non-CW LAA/LSPV alignment
- ↑ number of LAA particles
- 79% non-paroxysmal AF
- ↑ BNP
- ↓ LVEF
- ↑ creatinine
- ↑ ratio MPV/platelet count
- ↓ hematocrit

Saiz-Vivó et al., npj Digital Medicine 2025

Take-home messages – How to bring Virtual Humans from Academy to (real) Clinical Translation?

Don't think there is a unique formula

- What does "Clinical Translation" mean?
- I'm not very successful on this, anyway: 1/10 modelling projects.

Some likely relevant factors, from my experience

- Co-design, -develop, -validate with clinicians from the very beginning.
- Involve Key Opinion Leaders, bring them on board → then, industry will join.
- Modelling pipelines to process hundreds of cases.
- Verification, Validation, Uncertainty Quantification (and clear/useful QoI+CoU).
- Interfaces, interfaces, interfaces.
- An integrative solution, not only simulations (e.g., data management, visualization, report generation).
- Resilience → long journey traversing innovation territories!!

Short term future

- Regulation, Regulation, and Regulation.
- Training and planning contracts with device manufacturers.

PhySense research group (2011-Present)





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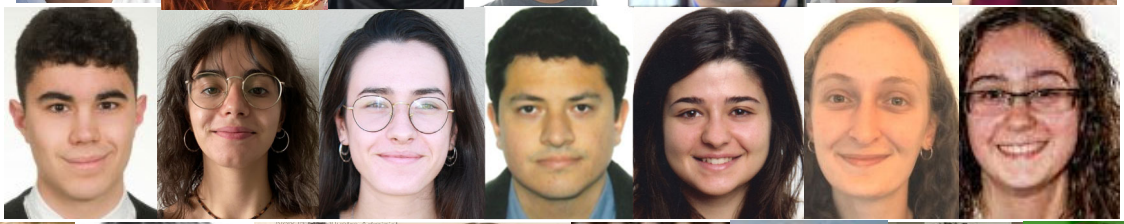
Manager / Tech transfer (1): Mònica Font

> 15 BSc/MSc thesis students

* External (5)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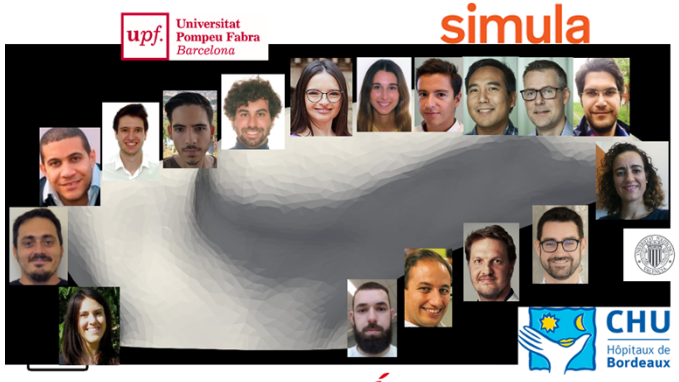

simula

SIM CARDIO TEST

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PhySense

Thanks for your attention