

Retos en la implantación sanitaria de técnicas computacionales avanzadas en medicina personalizada

**XI Conferencia Anual de las
Plataformas Tecnológicas de Investigación Biomédica**
Barcelona, 5th Marzo 2018

Oscar Camara

Physense, BCN-Medtech
Universitat Pompeu Fabra
oscar.camara@upf.edu





Brief overview of research career

My (main) research topics (2000-2007)

PhD (ENST Paris) on image processing, oncology

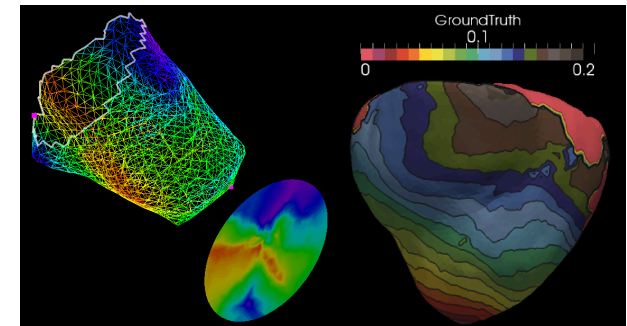
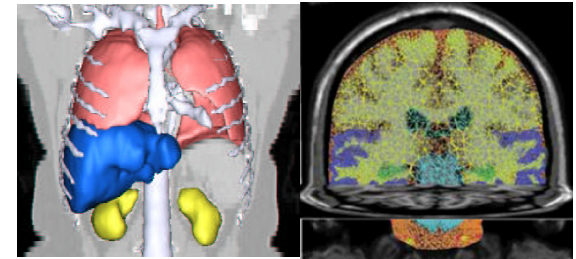
Postdoc (KCL, UCL) on modelling of AD

From 2007

RyC, associate professor (UPF)

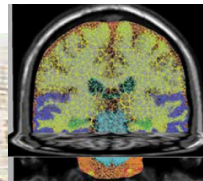
Personalized cardiac (EP) modelling

Cardiac data processing and integration



Segmentation;
Registration; Shape/
motion analysis

Imaging
Neurology



AD; Cerebral
aneurysms

Simulations
Cardiology

Personalization; Multi-
scale coupling

Heart Failure;
Arrhythmias; Foetal
circulation



What to do with this deluge of patient data?

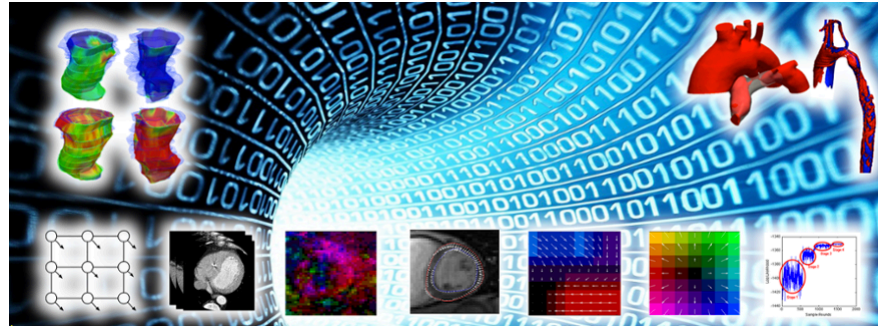
Dilbert



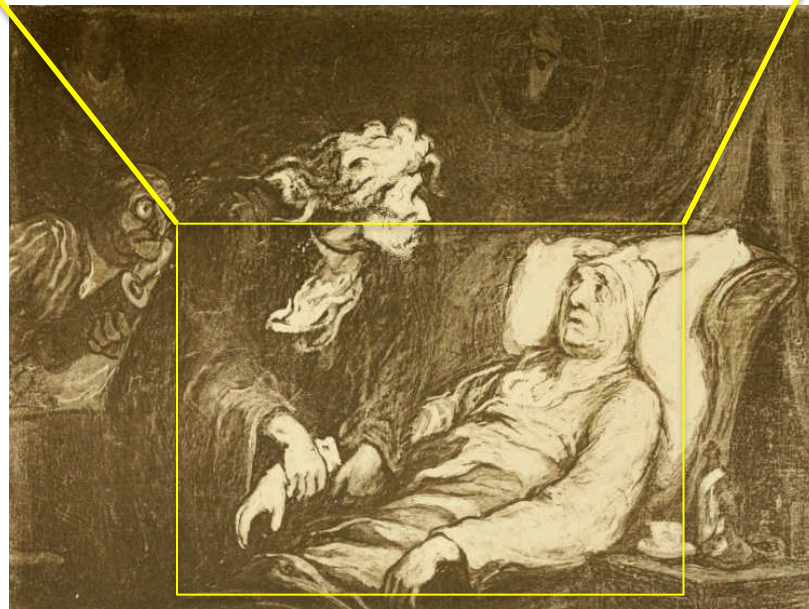
© Scott Adams, Inc.

Engineer

Big patient data



Carnegie-Mellon University



Patient

Doctora Juguetes



Clinician

Le malade imaginaire, Daumier, 1863



Data processing / integration / modelling

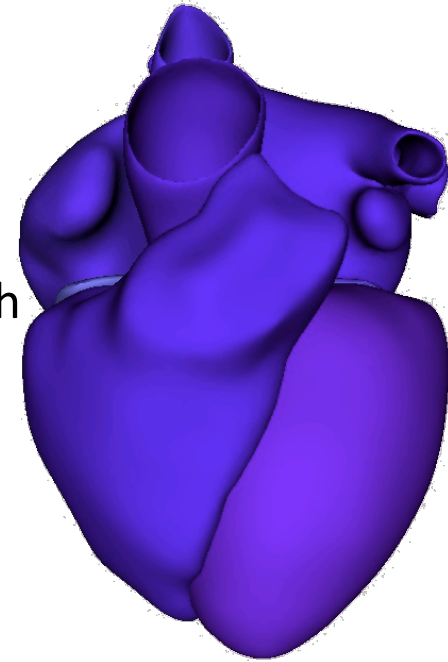


Processing

- Signal and image processing to extract indices of global and local function, geometry, shape, deformation

Integration

- All data corresponds to the same heart
- Each sensor offers sparse and specific information with an inherent (spatial & temporal) resolution and measurement error
- Mappings to common reference systems



Modelling

- Physiological models of electromechanics and haemodynamics



PhySense research group

Universitat Pompeu Fabra (UPF), Barcelona



P.I.'s (2): Oscar Camara (Associate professor),
Bart Bijnens (ICREA)

Postdocs (7): Constantine Butakoff, Marta
Guardiola, Andy Olivares, Patricia García, Judit
Chamorro, Ana González, Bruno Paun

PhDs (10): Marta Núñez, Cecilia Nunes, Sergio
Sánchez, Gabriel Bernardino, Federica Sacco,
Guillermo Jiménez, Irem Cetin, Rubén Doste,
Èric Lluch, Mariana Nogueira

Developers (2): Carlos Yagüe, Pilar García

Project manager (1): Marina Nicolas



Leitmotiv of PhySense



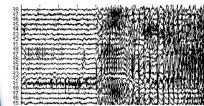
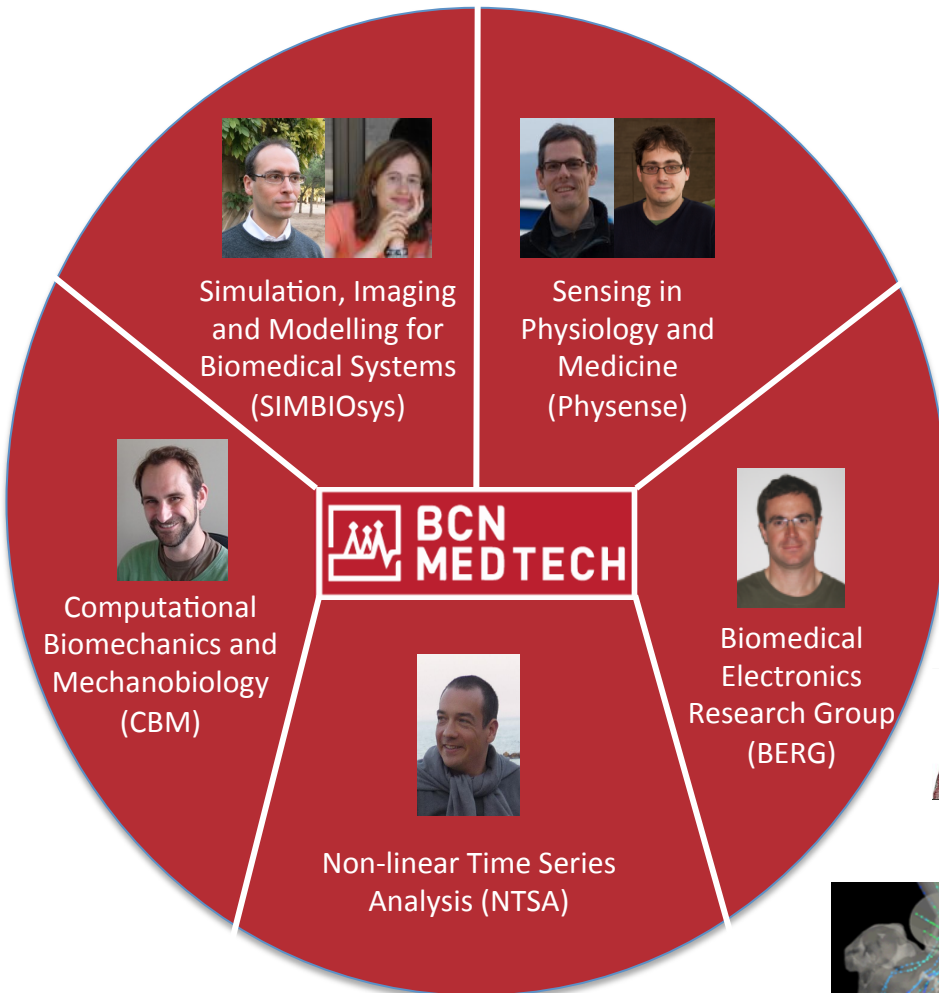
The main goal of **PhySense** is to **fill the gap** between engineers and clinicians, being a platform for **interdisciplinary** and **translational** biomedical engineering research with a strong focus on linking **technological** and **theoretical science** with **physiological** and **clinical knowledge** in internationally oriented excellent research



Barcelona Centre for New Medical Technologies

<https://bcn-medtech.upf.edu/>

Interdisciplinary and translational platform for
research in **biomedical engineering**



Computer Assisted Surgery

Medical Image Analysis

Biomechanics and Mechanobiology

Physiological Modelling

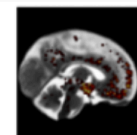
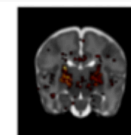
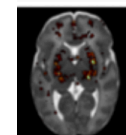
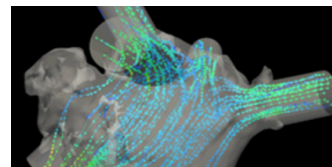
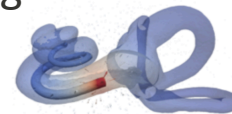
Biomedical Signal Processing

Biomedical Electronics

Biomedical Data Handling

Machine Learning

Clinical Translation





Challenges for clinical translation of advanced computational techniques

Machine Learning interpretability

Clinical (Big) data curation and management

Secure, remote and shareable access to data

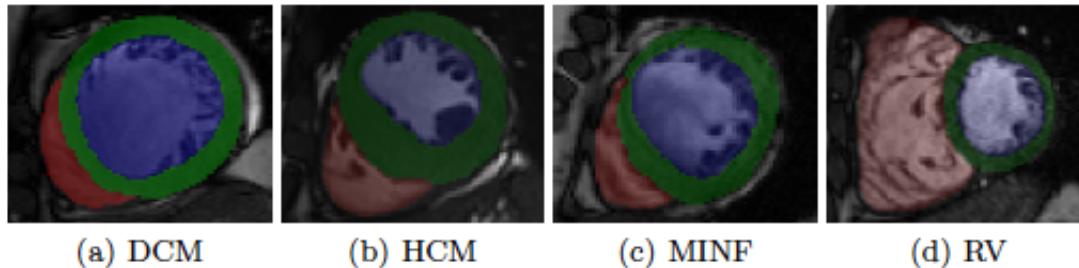
Simplification and validation of computational pipelines

Clinician-friendly interfaces

Access to advanced computational resources (e.g. HPC)



Radiomics approach to computer-aided diagnosis with cardiac cine-MRI



STACOM-MICCAI'17 challenge, 100 cases

Normal subjects (NOR).

Patients with dilated cardiomyopathy (DCM).

Hypertrophic cardiomyopathy (HCM).

Abnormal right ventricle (RV)

Myocardial infarction (MINF).

Advanced shape, texture features and demographics + SVM + feature selection

Using 5 radiomics features:

94% of accuracy

	NOR	DCM	HCM	MINF	RV
Precision	1	0.85	0.9	0.95	1
Recall	0.87	1	0.86	1	1

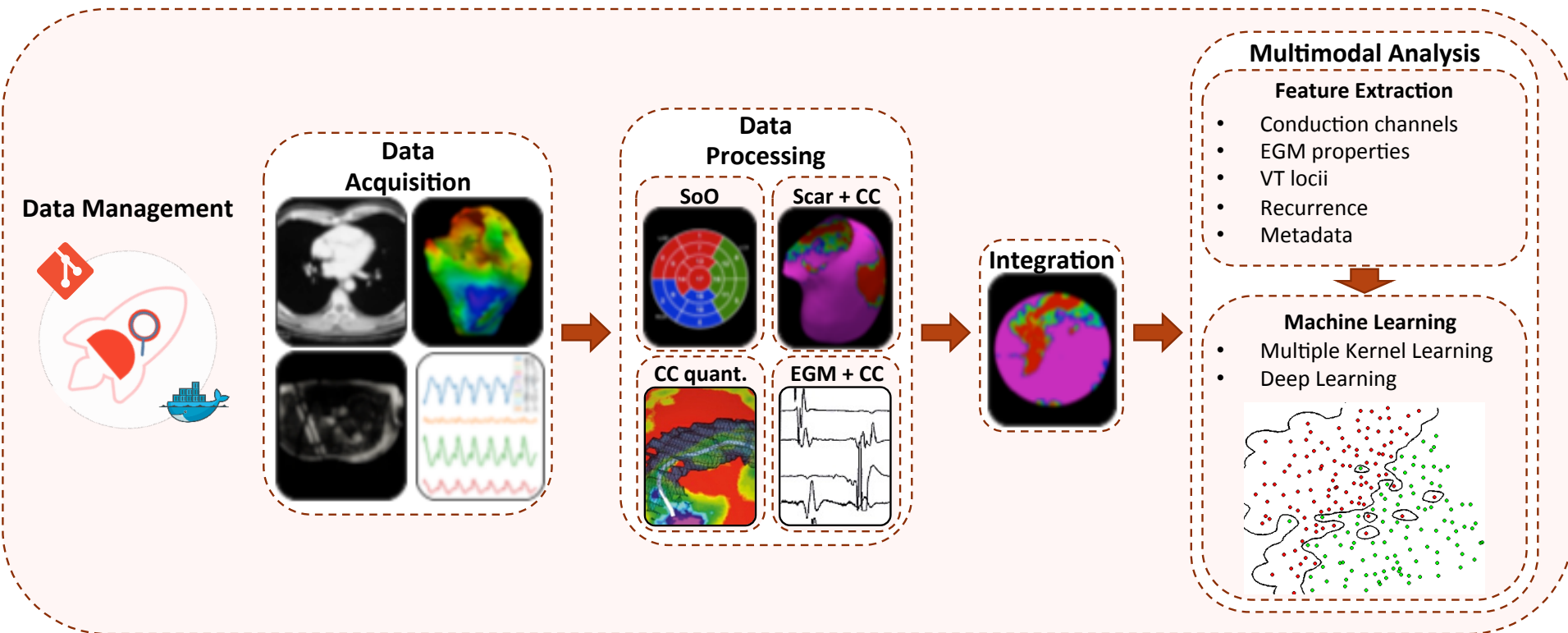
Using the best 10 features:

100% of accuracy

Name	Type	Frame	Structure	W/O	Alone
Volume	Conventional shape	ED	MYO	0.92	0.5
Surface Area to Volume	Advanced shape	ES	LV	0.88	0.62
Least Axis	Advanced shape	ES	LV	0.95	0.42
Maximum 2D diameter	Advanced shape	ED	LV	0.95	0.41
Maximum 3D diameter	Advanced shape	ES	RV	0.97	0.36
GLCM Inverse Difference	Intensity/textural	ES	RV	0.96	0.34
Compactness 2	Advanced shape	ES	LV	0.91	0.40
Maximum 3D diameter	Advanced shape	ES	MYO	0.96	0.47
Surface area	Advanced shape	ED	RV	0.97	0.29
Height	Patient Information	-	-	0.91	0.18



Machine Learning Techniques for the Joint Analysis of Multimodal Data from Substrate-Based Cardiac Arrhythmia Patients



Patient population: **1106 HF patients** ($LVEF \leq 30\%$, $QRS \geq 130$ ms, NYHA class $\leq II$) randomized to either CRT-D ($n=677$) or ICD ($n=429$) enrolled in MADIT-CRT

Model input

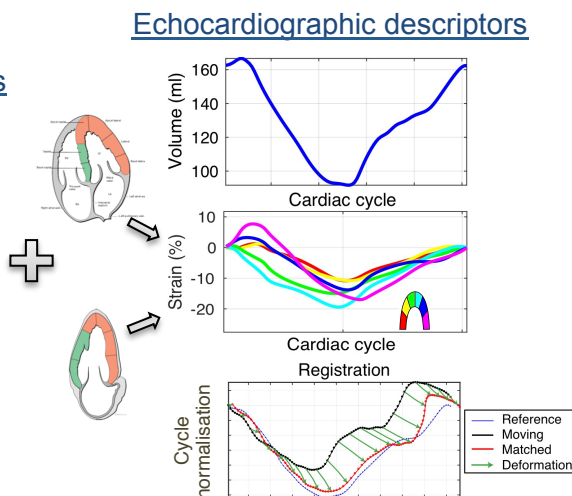
Clinical parameters

Continuous

Age	QRS width
LVEDVi	LAVi

Binary

Sex	Ischemic
LBbB	HF hosp.

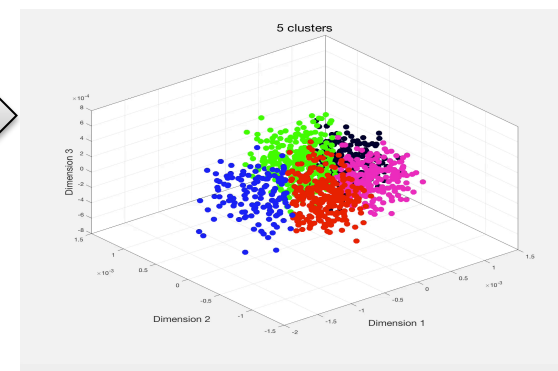
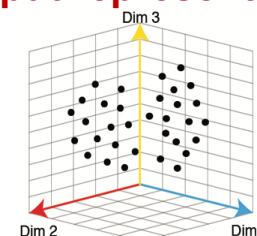


Unsupervised Multiple Kernel Learning (MKL)

Quantification of similarity

Dimensionality reduction

Output representation

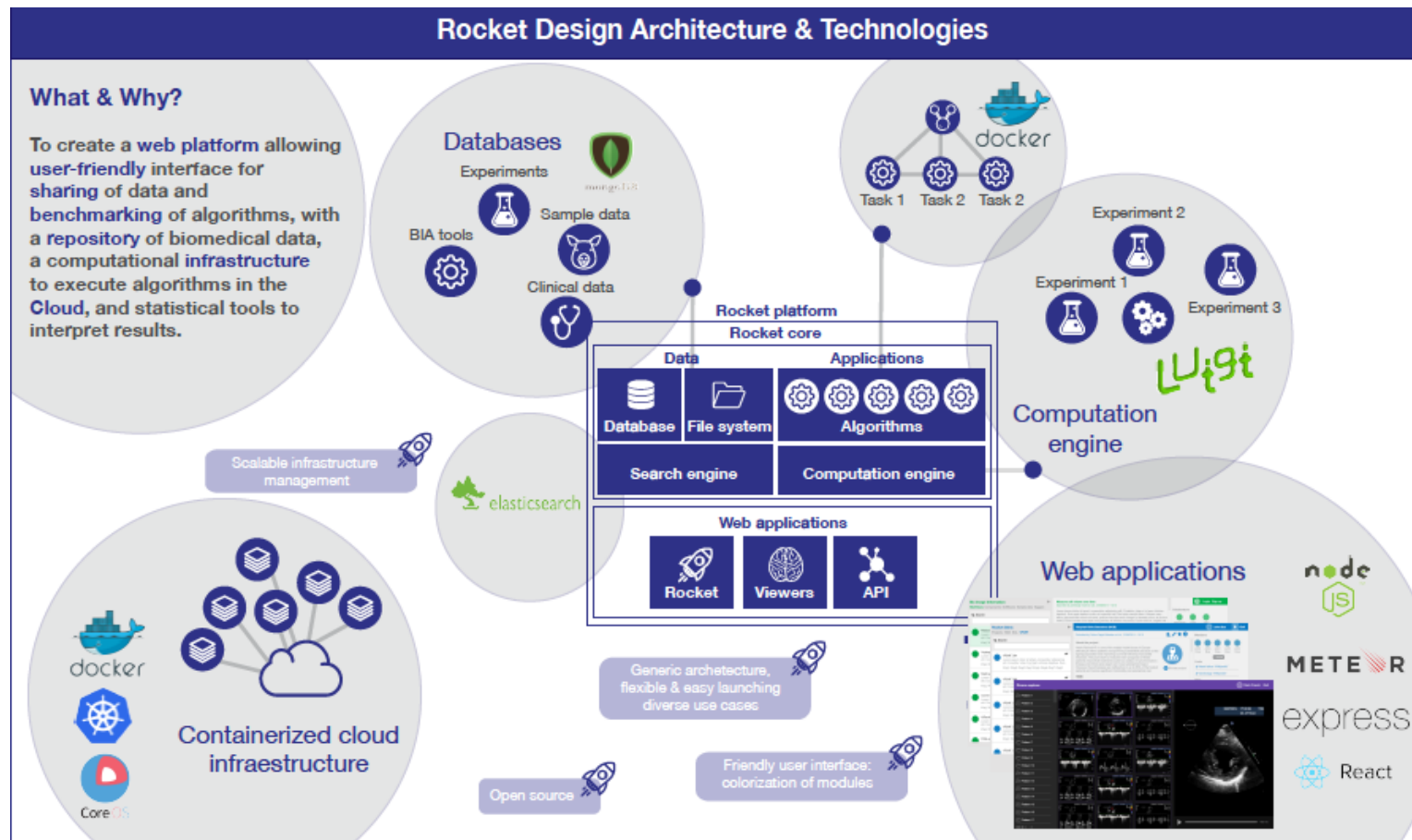


Aim: to **compare baseline characteristics, outcomes and treatment response** for the primary **outcome** (death or heart failure event) and **volumetric response** between clusters.

(Meta)data integration – The Rocket App



Main goal: to create a **web platform** allowing user-friendly **sharing of data** and **benchmarking of algorithms** with a **repository of biomedical data**, a computational infrastructure to execute algorithms in the **Cloud**, and statistical tools to **interpret results**



The Rocket App – Clinical use case

Clinical data of a patient

Different user access levels

Easy data importation/Exportation 

Data interpretation

Save data
Measurements, binaries,
quantifications ...

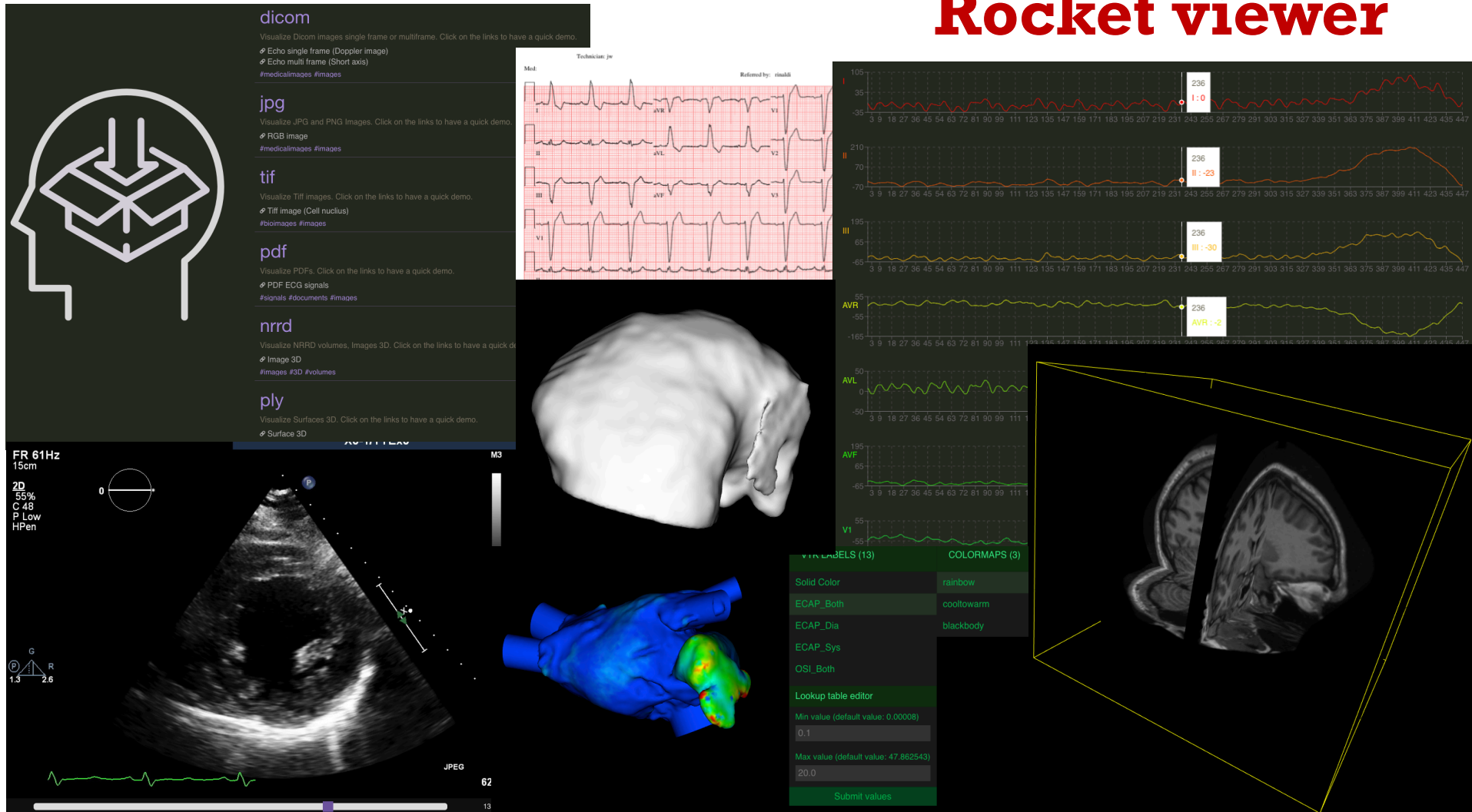
Process patient data through decision trees in order to predict a treatment

Visualize and process patient data

Fast overview of
highthroughput
images/signals



Web-based data visualization tool – Rocket viewer



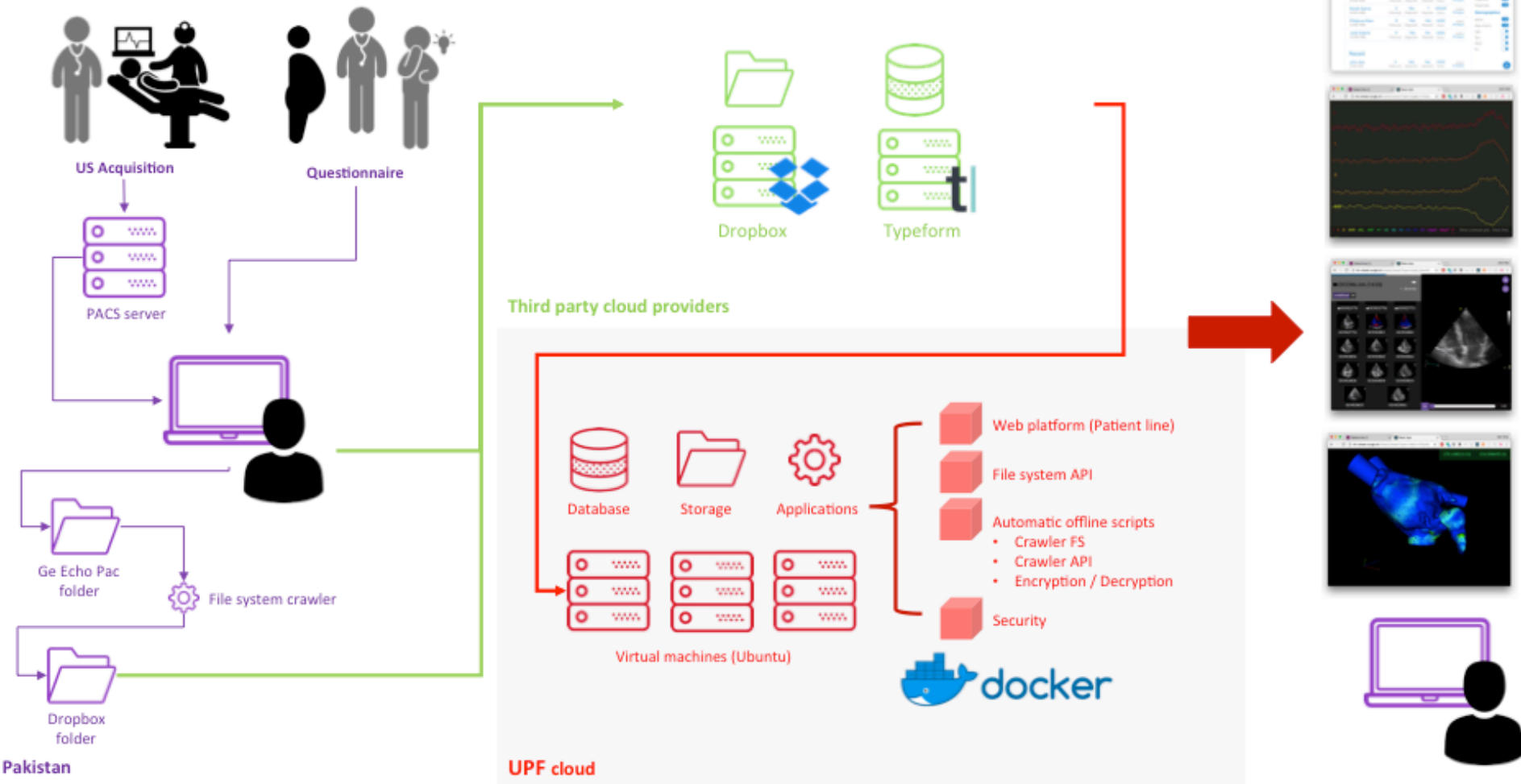
Youtube video: <https://www.youtube.com/watch?v=EGo5Roh2fca>



Machine learning based triage of foetal risk in underdeveloped countries



BILL & MELINDA
GATES foundation





**Ok, but computational models in
clinical routine?**



Let's back to 2008: euHeart project

Objective: develop, personalize and validate computational models of the heart to help diagnosis, treatment planning, interventions and the design of implantable devices

6 companies, 7 universities and research institutes, 5 hospitals

Duration of 4 years (2008-2012), budget of 19 millions of euros

Universities and research institutes

- INRIA, Sophia Antipolis, FR
- INSERM, Rennes, FR
- University of Karlsruhe, DE
- UPF, Barcelona, SP
- University of Sheffield, UK
- University of Oxford, UK
- Amsterdam Medical Center, NL

Industrial partners

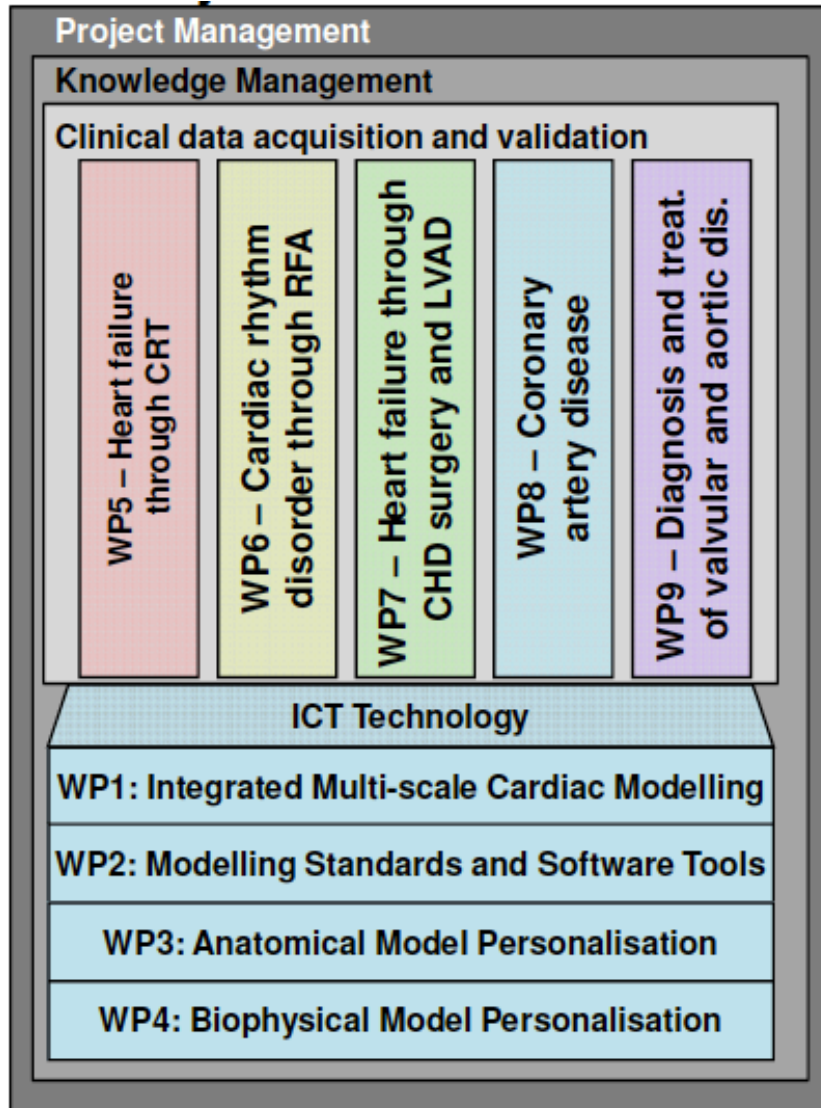
- Berlin Heart, DE
- HemoLab, NL
- Philips Healthcare, NL & SP
- Philips Research, DE
- PolyDimension, DE
- Volcano, BE

Hospitals and clinics

- KCL, London UK
- DKFZ, Heidelberg, DE
- INSERM, Rennes, FR
- HSCM, Madrid, SP
- Amsterdam Medical Center, NL



Let's back to 2008: euHeart project



Clinical Applications [WP5-9]

Vertical integration in five clinical applications with epidemiologically significance to evaluate clinical benefit of multi-scale modelling

Technical Development [WP1-4]

Economy of scale through development of generic technical solutions and horizontal integration of efforts

Clinical data acquisition and validation [WP10]

Clinical coordination at project level

Knowledge management [WP11]

Project management [WP12]

WHAT COULD

POSSIBLY GO WRONG?



euHeart project in 2012



- But applied to very limited amount of data ☹
 - Special thanks to patient KCL9

Medical Image Analysis 16 (2012) 201–215



Contents lists available at ScienceDirect

Medical Image Analysis

journal homepage: www.elsevier.com/locate/media



Patient-specific electromechanical models of the heart for the prediction of pacing acute effects in CRT: A preliminary clinical validation

M. Sermesant^{a,b,*}, R. Chabiniok^c, P. Chinchapatnam^b, T. Mansi^a, F. Billet^a, P. Moireau^c, J.M. Peyrat^a, K. Wong^a, J. Relan^a, K. Rhode^b, M. Ginks^b, P. Lambiase^e, H. Delingette^a, M. Sorine^f, C.A. Rinaldi^d, D. Chapelle^c, R. Razavi^b, N. Ayache^a

Med Biol Eng Comput

DOI 10.1007/s11517-013-1044-7

SPECIAL ISSUE - REVIEW

Understanding the mechanisms amenable to CRT response: from pre-operative multimodal image data to patient-specific computational models

C. Tobon-Gomez · N. Duchateau · R. Sebastian · S. Marchesseau · O. Camara · E. Donal · M. De Craene · A. Pashaei · J. Relan · M. Steghofer · P. Lamata · H. Delingette · S. Duckett · M. Garreau · A. Hernandez · K. S. Rhode · M. Sermesant · N. Ayache · C. Leclercq · R. Razavi · N. P. Smith · A. F. Frangi

Received: 24 April 2012 / Accepted: 2 February 2013

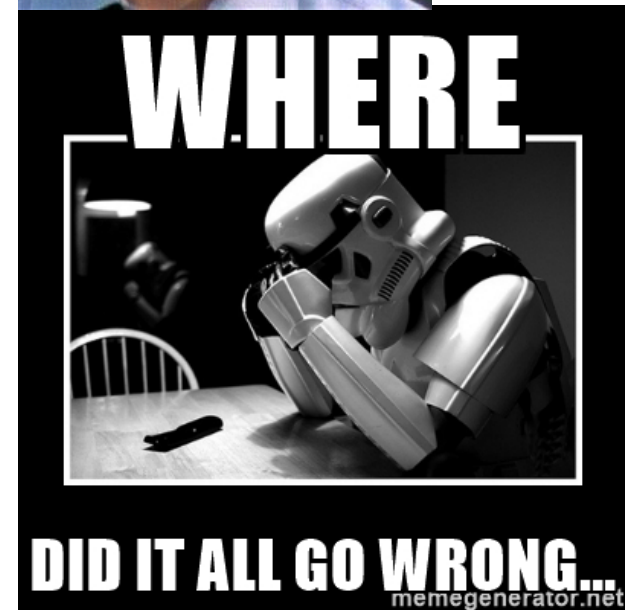
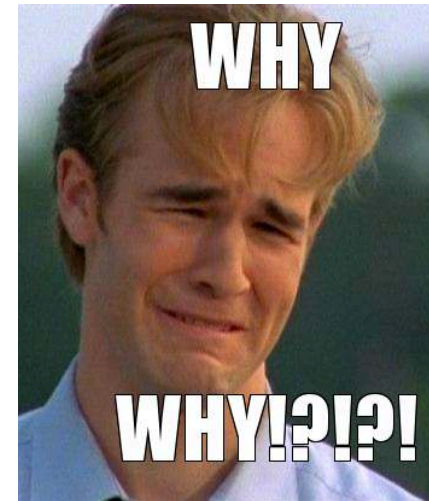
© International Federation for Medical and Biological Engineering 2013

on
2 patients

on
8 patients

PURE SPECULATION

- **Structural and communication issues** in such a large consortium
- **Not good enough data** (not necessarily acquired for research purposes)
- Computational models not advanced enough
- Computational techniques **not fast enough** for clinical routine
- **Limited computational resources**
- **Unclear clinical questions** or use
- Unclear idea by clinicians on limitations of computational techniques
- Bit of **overselling** the product





EU projects with usual suspects KCL, UPF, Inria, Philips, et al.

- From euHeart ...
 - 8 retrospective patients in 4 years ...

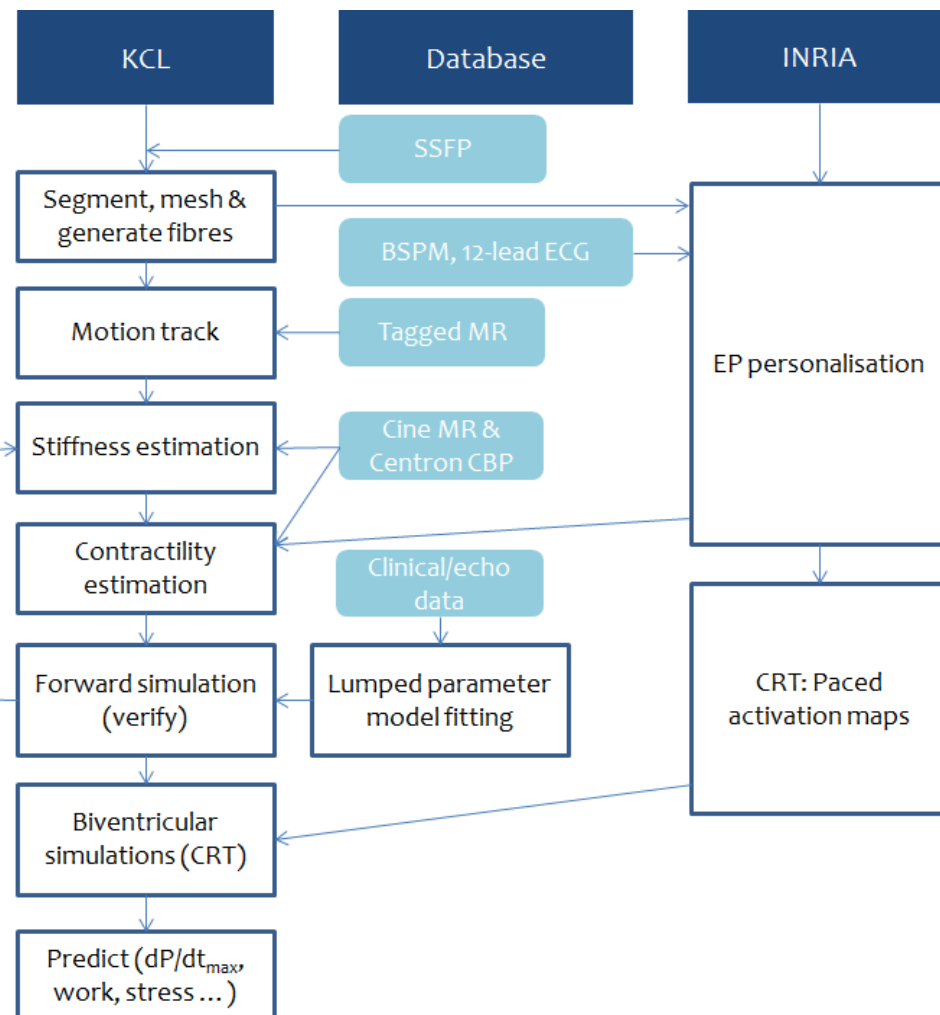
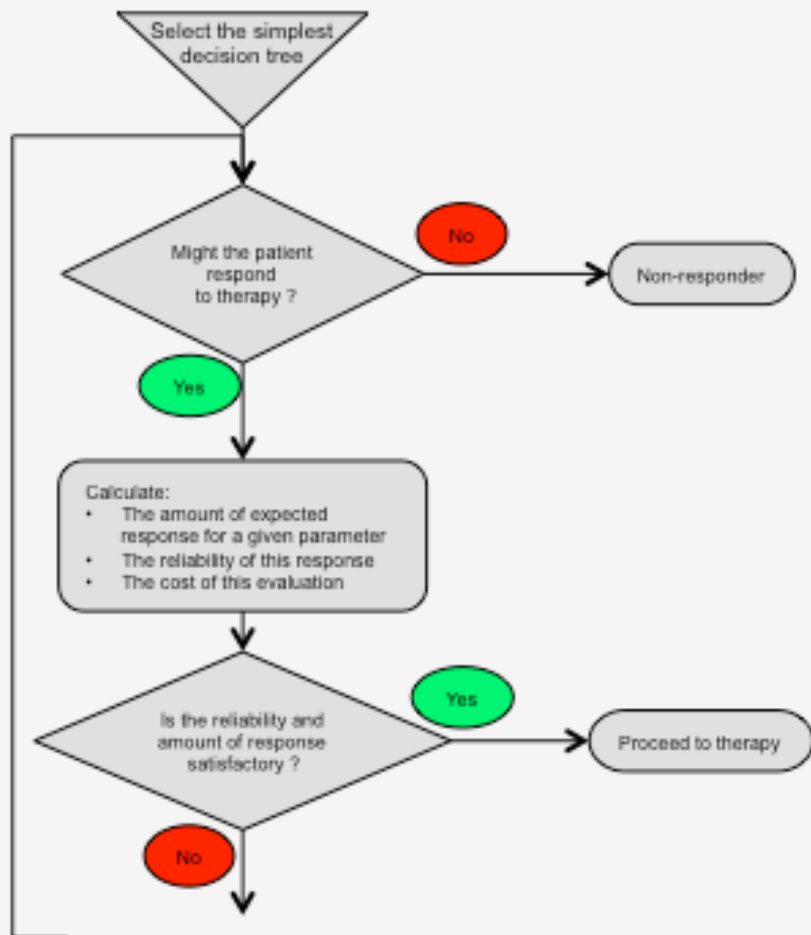


- ... to VP2HF
 - 1 patient every 2 weeks in a prospective study



EM simulations in 2 weeks after patient data acquisition

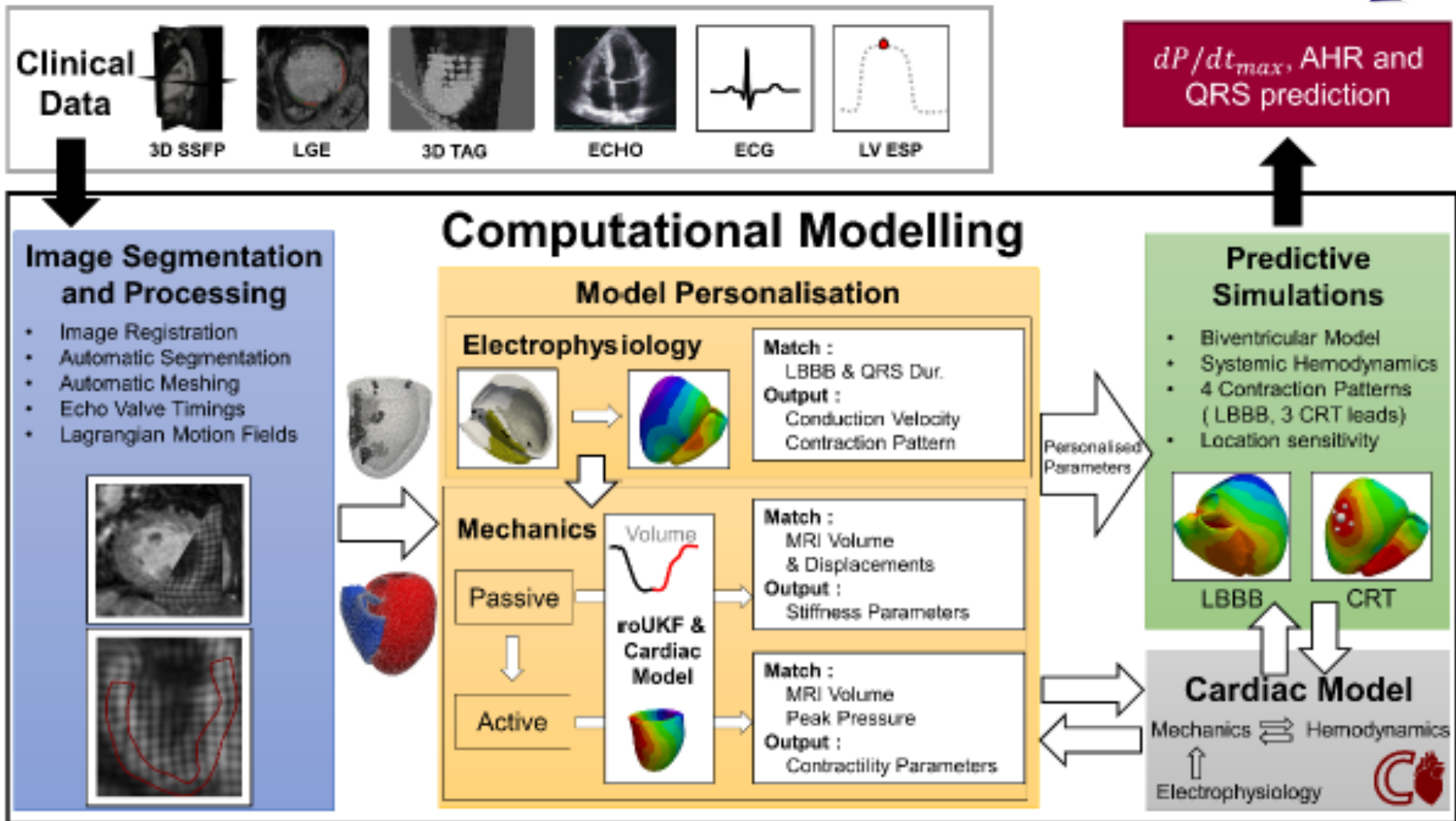
VP2HF decision algorithm





Cardiac computational models in the clinical workflow. We are doing it!! 😊

VP2HF



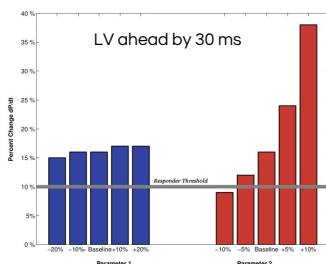
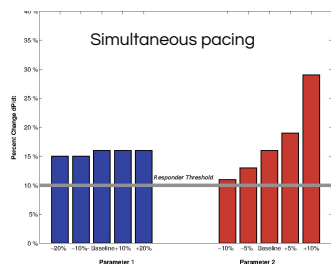
Simulation results in a clinician-friendly format

Decision Trees

Decision Tree	Patient Data	Outcome	PPV
ECG	QRS > 120, strict LBBB	Consider CRT	54%
Echo	no septal flash		
ESC	NYHA II, LVEF < 35%, QRS > 120	Consider CRT	53%
NICE	LVEF < 35%, QRS > 150	Consider CRT	57%

Conclusion

Prospective VP2HF decision is: **Model**



Pre-implantation

dpdt_{max} 901 ± 170 mmHg/s
EDP 12 mmHg
ESP 112 ± 8.8 mmHg
EDV 304 mL
ESV 235 ± 11 mL
EF 21.5 ± 4.8 %

Simultaneous Pacing

dpdt_{max} 1120 ± 320 mmHg/s
Δdpdt 18.5 ± 7.9 %
EDP 12 mmHg
ESP 110 ± 8.6 mmHg
EDV 304 mL
ESV 236 ± 11 mL
EF 22.3 ± 3.7 %

LV ahead by 30ms

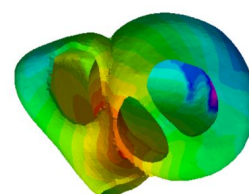
dpdt_{max} 1140 ± 340 mmHg/s
Δdpdt 19.8 ± 9.7 %
EDP 12 mmHg
ESP 111 ± 8.8 mmHg
EDV 304 mL
ESV 232 ± 11 mL
EF 23.6 ± 3.6 %

Modelling Prediction : Responder

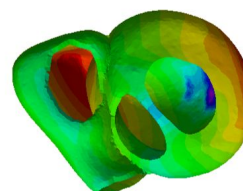
VP2HF_KCL_P001 Modelling Report

Report date: 27 Jan 2016

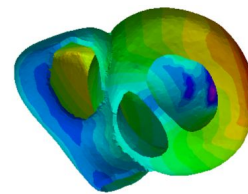
Study date: 12 Jan – 27 Jan 2016



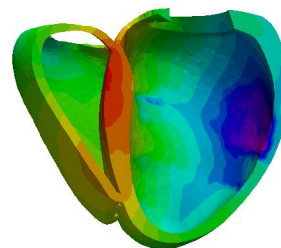
Baseline



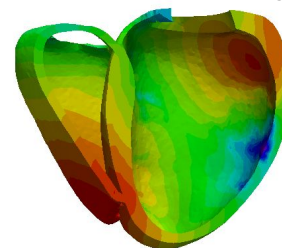
Simultaneous pacing



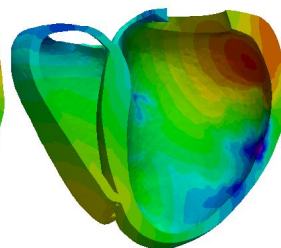
LV ahead by 30 ms



QRS = 161 ms

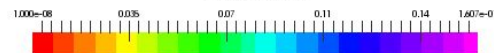


QRS = 145 ms

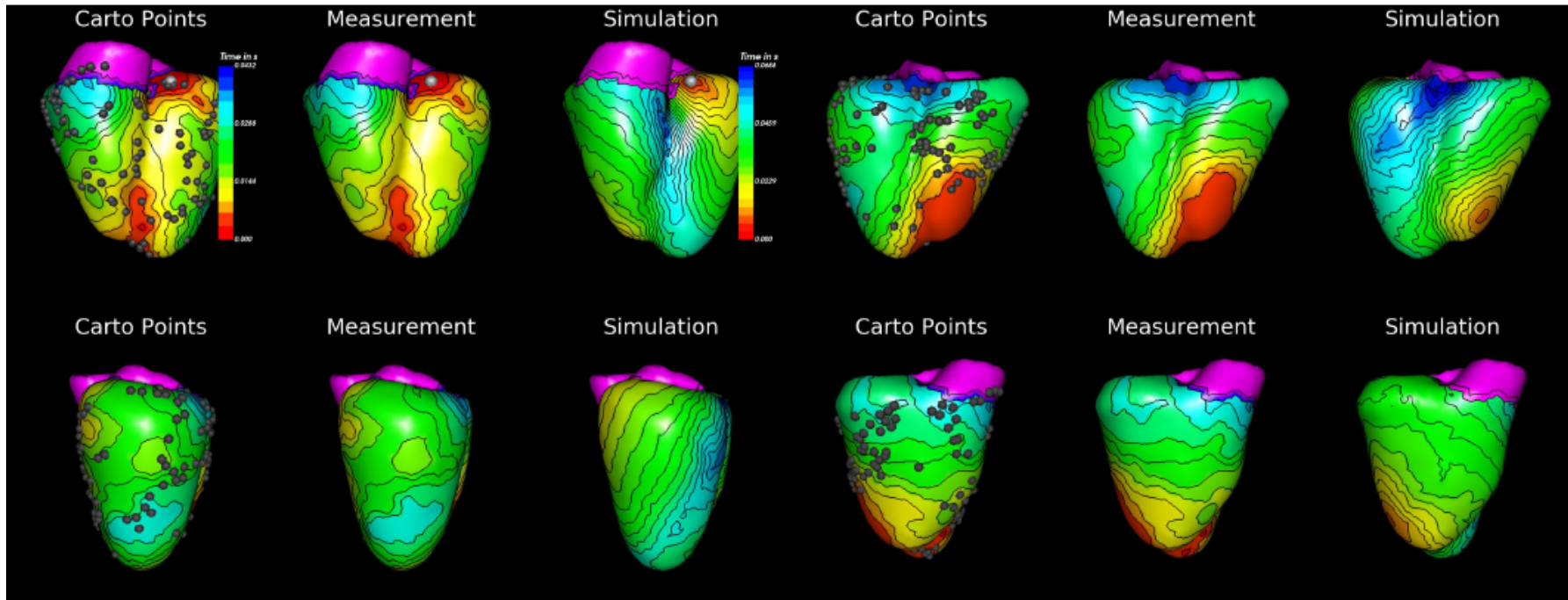


QRS = 149 ms

Depolarization time



Validation of EP simulations CRT prediction



	Whole: Global	Whole: Dense	LV: Global	LV: Dense	RV: Global	RV: Dense
Mean	12.4 ms	3.8 ms	9.1 ms	4.9 ms	12.0 ms	2.2 ms
Mean	13.9 ms	10.0 ms	25.1 ms	15.1 ms	25.6 ms	17.4 ms



PHILIPS



CLÍNICA
BARCELONA
Hospital Universitari



Materialise



Barcelona
Supercomputing
Center
Centro Nacional de Supercomputación



CFD modelling pipeline in COMPILAAO

Segmentation
LA, LAA in 3DRA data



Surface mesh
generation (triangles)

Export *.STL



Surface mesh
Taubin
smoothing



Meshlab



Remeshing : Clean
the free edges, bad
aspect ratio elements



Volumetric mesh
(tetrahedral) for the
fluid



gmsh



Surface mesh
processing: **Boolean
operations**



Manual determination of
pulmonary veins (PVs) and
mitral valve (MV)

CFD
simulations



Post-processing:
Paraview

ANSYS

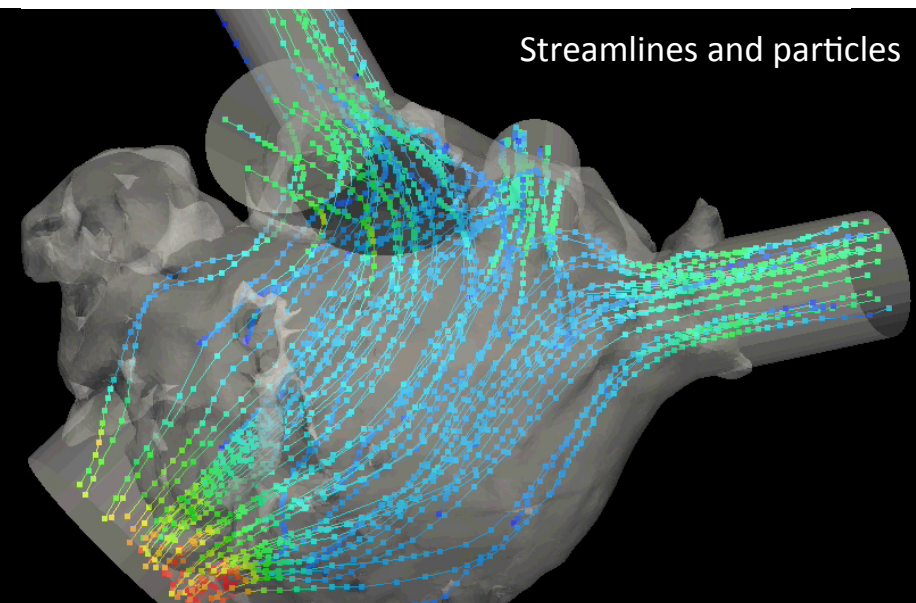
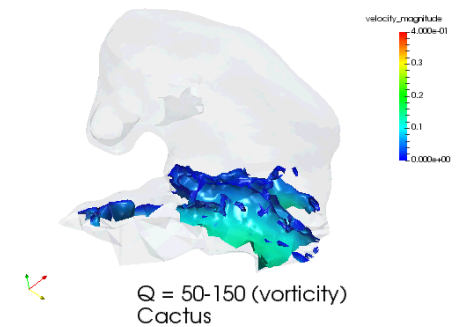
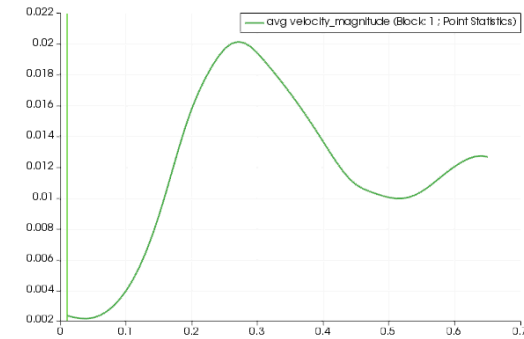
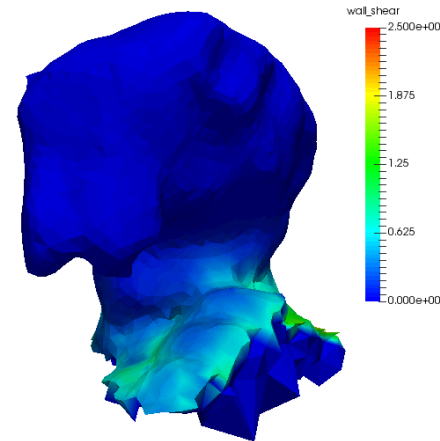
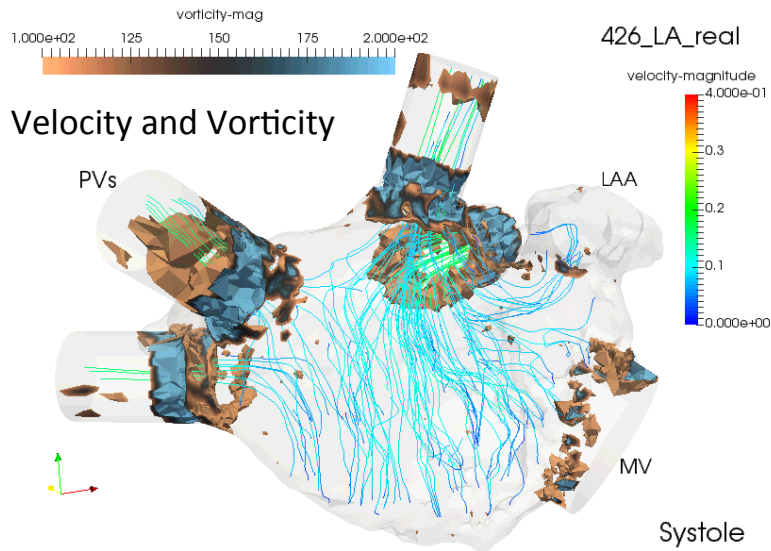
Alya
HPCM

OpenFOAM

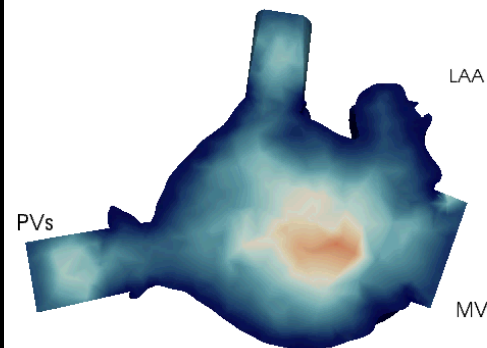
ParaView



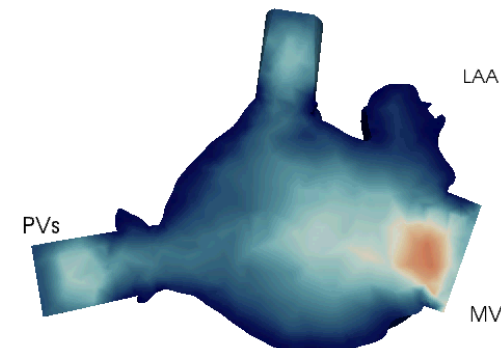
Joint analysis of LAA morphology and haemodynamics



Reynolds systole



Reynolds diastole





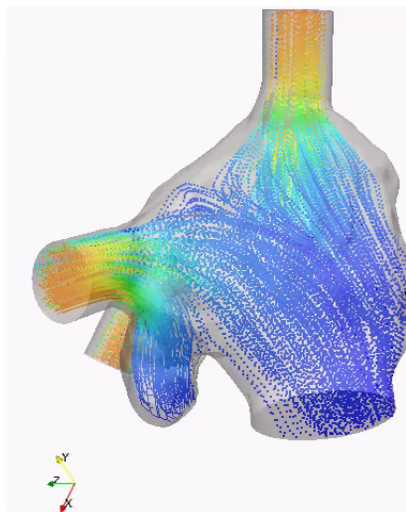
Preliminary work. Virtual deployment of (LAAO) devices



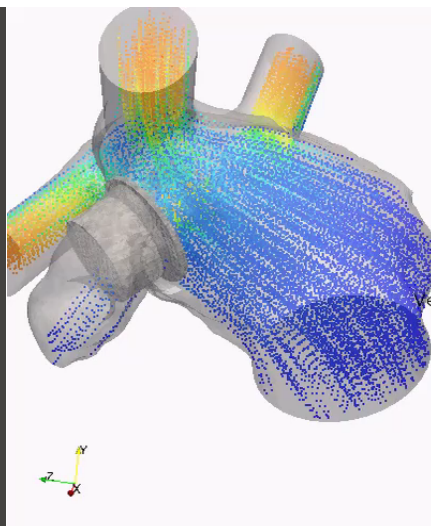
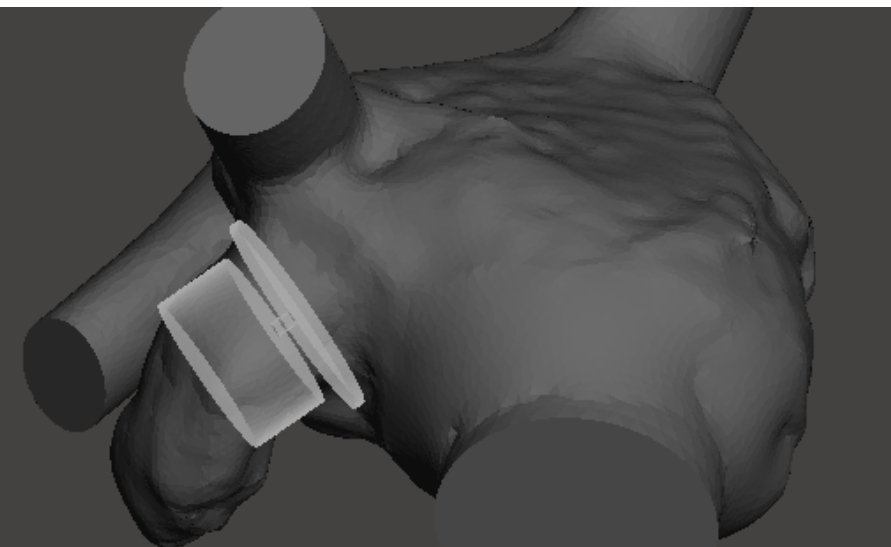
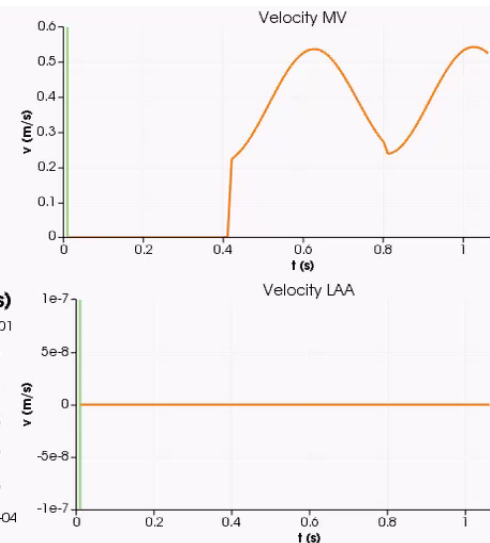
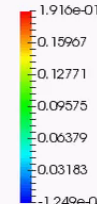
WATCHMAN™



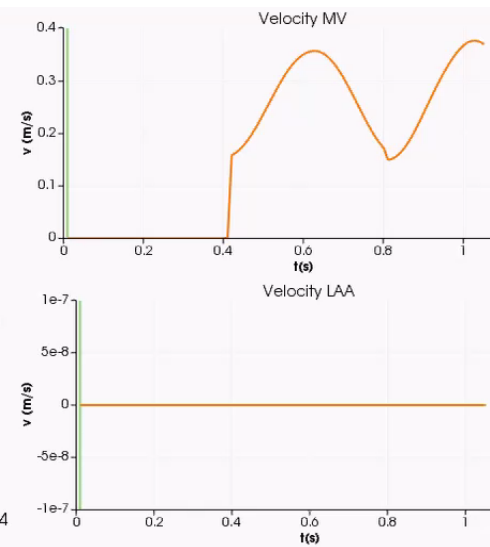
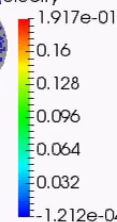
AMPLAZER™ Amulet™



Velocity (m/s)



Velocity



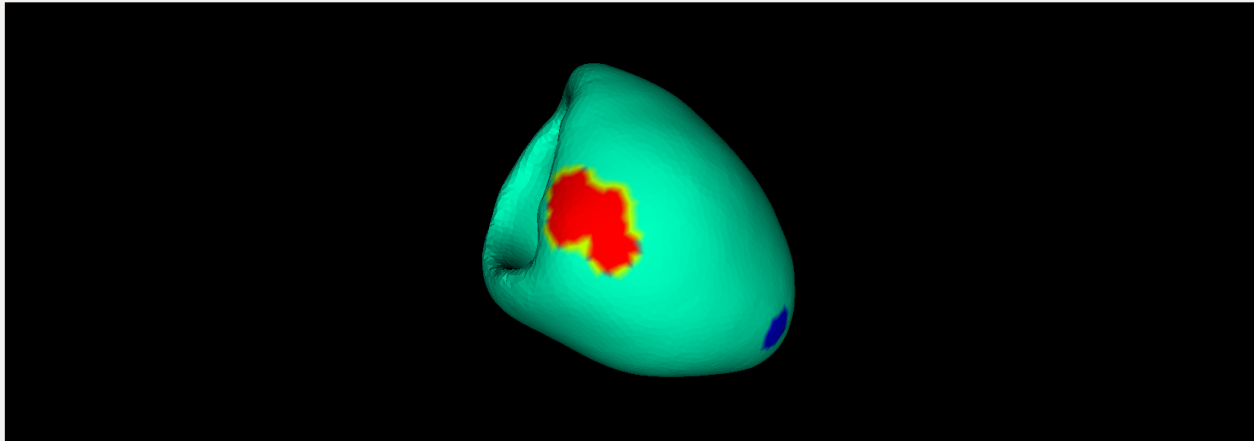


Electromechanical models of the heart with meshless (SPH) methods



Cardiofun♥ion

Program to prepare mesh to run electrical simulation. The simulation will run when the window is closed.

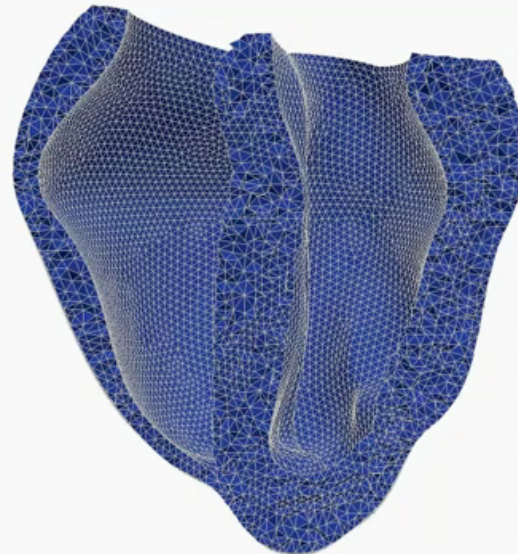


Buttons to modify parameters

Tissue type	healthy
Cond. Coeff.	1800
TauOpen [s]	120e-3
TauClose [s]	150e-3
TauIn [s]	3e-4
TauOut [s]	6e-3
Vgate [mV]	0.13
Iapp [Hz]	2000
Time step [s]	1e-4
Total time [s]	1.5

Update

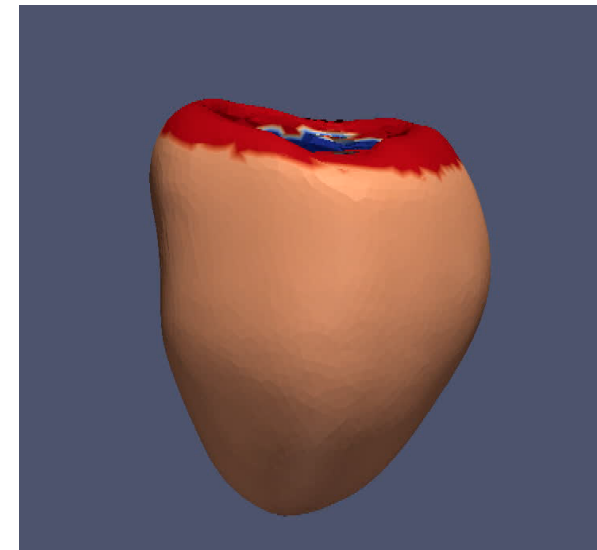
Buttons to modify mesh properties. Initial impulse is added by default.



Interface
being used
by
clinicians
at Philips



SPH-based
snow





Red Española de Modelización Computacional Cardíaca



VHEARTSN

Red Española de Modelización
Computacional Cardíaca

Universitat Politècnica de València
Universidad de Navarra
Universitat de València
Universitat Politècnica de Catalunya
Basque Center for Applied Mathematics
Universitat Pompeu Fabra
Barcelona Supercomputing Center
Universidad de Zaragoza



Universidad
de Navarra



**Barcelona
Supercomputing
Center**
Centro Nacional de Supercomputación



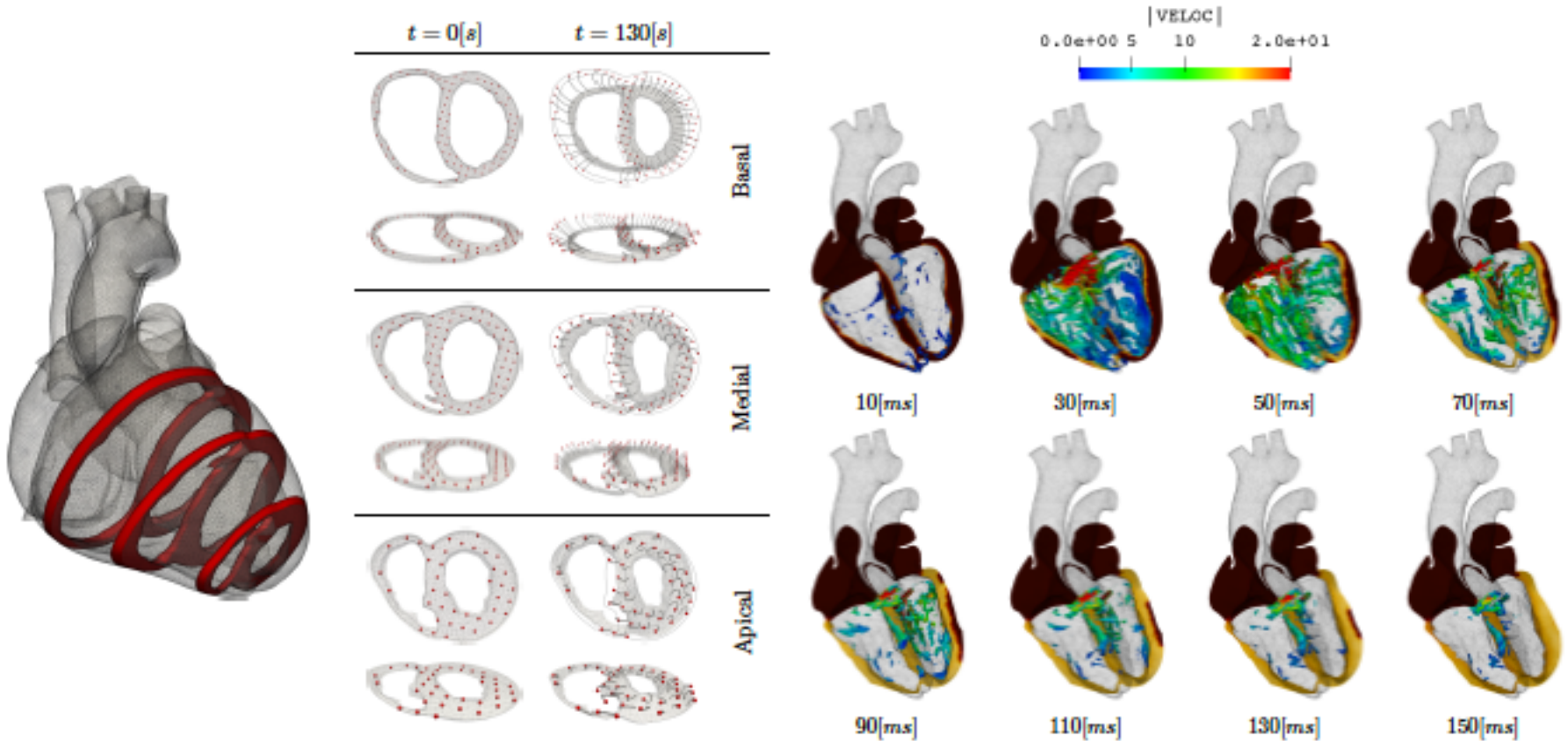
**Universidad
Zaragoza**



VHEARTSN aims at facilitating and accelerating the development, implementation and application of computational models in biomedical research

- Increase contact of engineers with doctors and companies
- Use of computer models in daily clinic through access to HPC resources
- Support design of personalized therapies and devices

HPC-based cardiac simulations with Alya – BSC. PhD of Alfonso Santiago (22/03/2018)





Conclusions - Challenges for clinical translation of advanced computational techniques

Machine Learning interpretability → **careful with black boxes**

Clinical (Big) data curation and management → **engineers needed in the hospital for data management**

Secure, remote and shareable access to data → **need for advanced infrastructure**

Simplification and validation of computational pipelines → **otherwise, impossible clinical translation of tools**

Clinician-friendly interfaces → **need of visual analytics, user-guided processes, portable and interactive tools**

Access to advanced computational resources (e.g. HPC) → **improve awareness of clinicians; strategic alliances between academia, hospitals and industry**

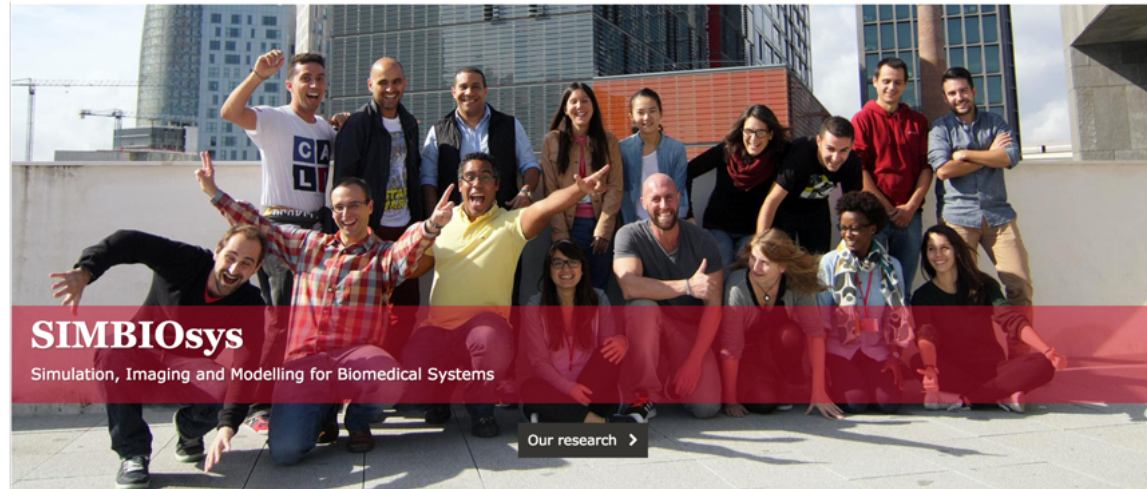


Acknowledgments

- PhySense, Simbiosys
- BCN MedTech
- euHeart, VP2HF, CardioFunXion partners and funding agencies
- Clinicians (H. Clínic, St. Thomas, ...)

Other colleagues:

Rafa, Ali, Dani, Mariano, Jaz, Javier, Pablo, Juan Pablo, Alex, Damián, Rob, Kawal, Anders, Cata, Tommaso, Daniel, ...



Thanks for your attention