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







# CARDIAC RISK ASSESSMENT MOXIFLOXACIN + ONDANSENTRON + DOFETILIDE CLINICAL COMPARISON





COMPARISON WITH DARPO ET AL . , 2015



# CARDIAC RISK ASSESSMENT OBSERVED ARRHYTHMIC BEHAVIOUR

 LBBB produced in a female subject after the administration of 800 mg of HCQ.





# MODEL INPUTS: SYNTHETIC PATIENT FROM OUR DATABASE PM IMPLANTATION POSITION

| Case    | depol. time | LV-EF     | LV-ESV        |
|---------|-------------|-----------|---------------|
| Healthy | 120 [ms]    | 56 %      | $49 \ [cm^3]$ |
| LBBB    | 400 [ms]    | 19 %      | $91 \ [cm^3]$ |
| CRT10   | 250 [ms]    | $40 \ \%$ | $67 \ [cm^3]$ |
| CRT40   | 230 [ms]    | 42 %      | $65 \ [cm^3]$ |
| CRT80   | 230 [ms]    | 44 %      | $63 \ [cm^3]$ |





# LEFT BUNDLE BRANCH BLOCK CARDIAC RESYNCHRONISATION THERAPIES



#### PACEMAKER MOTION CURVES



# ATRIOVENTRICULAR BLOCK CARDIAC RESYNCHRONISATION THERAPIES







### Q-CRITERION





20 CRT REAL PATIENTS FROM H. STPAU, BARCELONA

EXPANDED TO 350+ VIRTUAL PATIENTS

STATISTICAL ANALYSIS ON THE VIRTUAL COHORT, COMPARED TO THE REAL ONES

ACUTE SCENARIO: ANALYZING **BIOMARKERS JUST BEFORE AND AFTER** PACEMAKER IMPLANT

BIOMARKERS ANALYZED: QRS LENGTH, ECG MORPHOLOGY, EJECTION FRACTION, ۰Ŀ., END OF SYSTOLE VOLUME, STRAINS PER AHA SEGMENT,...

# CRT INSILICO CLINICAL STUDY WITH SANT PAU HOSPITAL **ONGOING STUDY**







#### POST CRT



Ε.

PRE CRT



















### SENSITIVITY MATRIX INPUTS VS. BIOMARKERS





### HEATMAP **BIOMARKERS VS.** PATIENTS

| 1000-01123-0100-01                       | 764 755 754    | 10722 1.54 1.44                    | 1.58 1.54 5.65 | 4.215 0.309 4.33        | 10.3 34 15.5   | 5.58 5.50 5.5  | 3.427 0.421 0.43  | 29 18.5 27.7                  | 57 549 534     | tan tar-       |
|--|----------------|------------------------------------|----------------|-------------------------|----------------|----------------|-------------------|-------------------------------|----------------|----------------|
| 1000-01171-01200-01                      | 40.0 10.4 10.1 | 12.0 11.2 13                       | 4.31 4.43 4.57 | 6.25 (129- <b>1</b> 475 | 86 81 87       | 3.79 3.80 4.54 | 3.500 0.000 0.000 | 417 42.8 91.8                 | 4.00 4.74 4.78 | 121-1214       |
| Employation                              | 664 363 654    | 12.8 10.8 20.2                     | 4,25 4.45 4.57 | 4.22 0.226 6.24         | 01.0 101 00    | 341 343 348    | 1211 1200 1270    | en en 182                     | 1.82 4.8 4.08  | 1.10 1.10      |
| Jannessen                                | 264 158 411    | 4.56 6.57 7.58                     | 4.01 4.01 4.7  | 6.86 1.11 0.206         | 309 268 209    | 4.43 4.17 4.55 | 1.02 0.020 0.107  | 817 162 167                   | 4.00 4.0 4.01  | 100 1270       |
| Employation more                         |                | 12.4 10.5 10.1                     | 1.00 1.00 1.00 | eam part pare           | 49.3 47.4 45.7 | 3.27 5.29 3.21 | 1073 0071 0.075   | 817 969 963                   | 43 434 437     | 111 111        |
| E meret and a second                     | and 201 and    | 21.4 ISA ISA                       | 35 455 4.52    | 6 60 (0 17) (0 16)      | 1816 EF# 10.5  | 3.15 3.27 3.66 | 3208 0309 0338    | 81.0 00 30.0                  | 4.00 4.00 4.04 | 1100104        |
| E 2010 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 | 364 255 411    | 11.8 10.7 11.7                     | 430 418 434    | e ani 1 26 1 200        | 488 497 497    | 3.00 3.00 3.05 | 1200 0200 0.17    | N                             | 4.10 4.32 4.21 | 0.140 0.140    |
| 2010/01/1714 01000                       | HE 162 16.1    | 21.1 21.8 26.8                     | 3,86 4,97 4,93 | 0.16 0.16 0.172         |                | 2.1 3.25 3.45  | 126.076.039       | ALS M.2 M12                   | 4.10 4.30 4.47 | 118 111        |
| 200-0127-040-0                           | 463 BK 861     | M.1 M.8 20                         | 179 189 4.17   | 6.120 (0.14 (0.146      | 16 017 16.4    | 3.15 5,27 3.66 | 1208 0 209 0 200  | 81.0 80 80.0                  | 158 419 415    | 6.11 2.154     |
|  | 16 Ú 12        | * 0 0                              | 6 Q Q          | 6 0 Q                   | မ်းမိုးမ       | 6 0 0<br>1     | 6 D U             | 6 U U                         | 6 0 U          | 54 LC<br>16    |
|  |                |                                    |                |                         |                |                |                   |                               |                |                |
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# LEFT VENTRICULAR ASSIST DEVICE THROMBOGENESIS STUDY WITH FDA AND SDSU



#### Young = 6e5 dyna/cm^2

IMMERSED BOUNDARY METHOD ON ARBITRARY LAGRANGIAN EULERIAN WITH ANISTROPIC MESH REFINEMENT (IBM+ALE+AMR)

MULTI-MATERIAL BIOPROSTHETIC VALVES



<u>i - i</u> Time: 0.147000s

Young = 3e7 dyna/cm/2





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Barcelona Supercomputing Center



# MODEL INPUTS: ■ LEAFLET MATERIALS ■ FLOW CONDITIONS GOALS: CREATE A "V.LAB" FOR VALVE IMPLANTS COMPUTE FLOW BIOMARKERS FOR THROMBOGENESIS CHECK LEAKING UNDER DIFFERENT FLOW, POSITION AND CUSP MATERIALS AND DESIGN

**BIOPROSTHETIC AORTIC** VALVES





| Biomarkers |  |
|------------|--|
|            |  |
|            |  |
|            |  |

# THE RESPIRATORY SYSTEM

### COLLABORATORS:





HOSPITAL CLINIC (SPAIN) RMIT (AUSTRALIA) NATIONAL INSTITUTE OF TECHNOLOGY, GIFU COLLEGE (JAPAN) IMPERIAL COLLEGE LONDON (UK) FLUIDDA (BE) NORTH CAROLINA STATE UNIVERSITY (US) NORTHROP GRUMMAN CENTER FOR HPC, JACKSON STATE UNIVERSITY (US) UNIVERSITAT POMPEU FABRA (SPAIN) CINCINNATI CHILDREN HOSPITAL



CALMET, H., GAMBARUTO, A.M., BATES, A.J., VÁZQUEZ, M., HOUZEAUX, G. AND DOORLY, D.J., 2016. LARGE-SCALE CFD SIMULATIONS OF THE TRANSITIONAL AND TURBULENT REGIME FOR THE LARGE HUMAN AIRWAYS DURING RAPID INHALATION. COMPUTERS IN BIOLOGY AND MEDICINE, 69, PP.166-180.





# ALYA PURPLE: THE VIRTUAL PREGNANCY LAB

COLLABORATORS:







### WASHINGTON UNIVERSITY ST. LOUIS



Barcelona Supercomputing Center Centro Nacional de Supercomputación

#### 4.0e+01



-8.60+0



#### RESPIRATORY SYSTEM



### VIRTUAL PREGNANCY LAB



#### CARDIAC VALVES



# OUR VISION THE HUMAN DIGITAL TWIN



### INTERVERTEBRAL DISK













# CONCLUSIONS & FUTURE LINES







# NOW & TOMORROW

HIGH PERFORMANCE COMPUTING IS NOT NEEDED EVERYWHERE IN THE BIOMEDICAL REALM ...

... BUT FOR SOME (MANY) PROBLEMS IT IS THE ONLY WAY

HPC IS MATURE ENOUGH TO BE USED: MATHEMATICAL MODELS **LOAD BALANCING TECHNIQUES** PROGRAMMING MODELS HARDWARE AND ITS AVAILABILITY SOFTWARE AND ITS AVAILABILITY INPUT DATASETS...





# **ALGORITHMS, SOLUTION SCHEMES, IMPLEMENTATION STRATEGIES**

# NOW & TOMORROW

HIGH PERFORMANCE COMPUTING IS NOT NEEDED EVERYWHERE IN THE BIOMEDICAL REALM ...

... BUT FOR SOME (MANY) PROBLEM NDS THE ONLY WAY

HPC IS MATURE ENOUGH TO BE USED: **LOAD BALANCING TECHNIQUES** PROGRAMMING MOITELS HAPPENING NOW HARDWARE AND ITS AVAILABILITY SOFTWARE AND ITS AVAILABILI INPUT DATASETS...





# THIS IS ALGORITHMS, SOLUTION SCHEMES IMPLEMENTATION STRATEGIES MATHEMATICAL MODES

# NOW & TOMORROW A LOT TO BE DONE ON INCREASING **CONFIDENCE** IN THESE TOOLS...

# ... BUT LOOK AT OTHER FIELDS NOW! (AEROSPACE, ENERGY, CLIMATE...) BOTH INDUSTRY AND GOVERNMENT TO FUEL THE PACE (LEARN

# COVID-19 LESSONS)

# MORE **HANDS** NEEDED: CLINICAL AND MEDICAL INSIGHT MATHEMATICAL MODELLING (NOT JUST A!!) COMPUTER SCIENCE EXPERTS CO-DESIGN WITH HARDWARE ARCHITECTS





# SUPERCOMPUTER-BASED IN-SILICO CLINICAL TRIALS

MARIANO VÁZQUEZ CSO/CTO – ELEM BIOTECH TEAM LEADER – BARCELONA SUPERCOMPUTING CENTER

# ELEM

THE VIRTUAL HUMANS FACTORY





# To pose a question, you can write your question in the "Questions" tab



is project has received funding from the European Union's prizon 2020 research and innovation programme under grant agreement No 823712







https://insilicoworld.slack.com/ archives/C0151M02TA4

The e-Seminar series is run in collaboration with:





# **Thank you for participating!**

# ...don't forget to fill in our feedback questionnaire...



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# InSilicoWorld Community of Practice

# Expertise

- The community is invitation only: in this way we ensure only interested experts have access

# Collaboration

– Join teams and collaboratively work on shared goals, projects, concerns, problems or topics

# Safe space

- A pre-competitive space where experts from academia, industry, and regulatory agencies can ask for and exchange advices



The first community entirely on in silico medicine www.insilico.world/community

More than 500 experts have already joined the community and its channels

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