TOR VERGATA
UNIVERSITÀ DEGLI STUDI DI ROMA

Avicenna Alliance
Association for Predictive Medicine

Enabling the Medical Digital Twin by advanced mesh morphing and high fidelity patient-specific simulations

Prof. Marco E. Biancolini

Associate Professor at **UTV**

Founder at **RBF Morph srl**

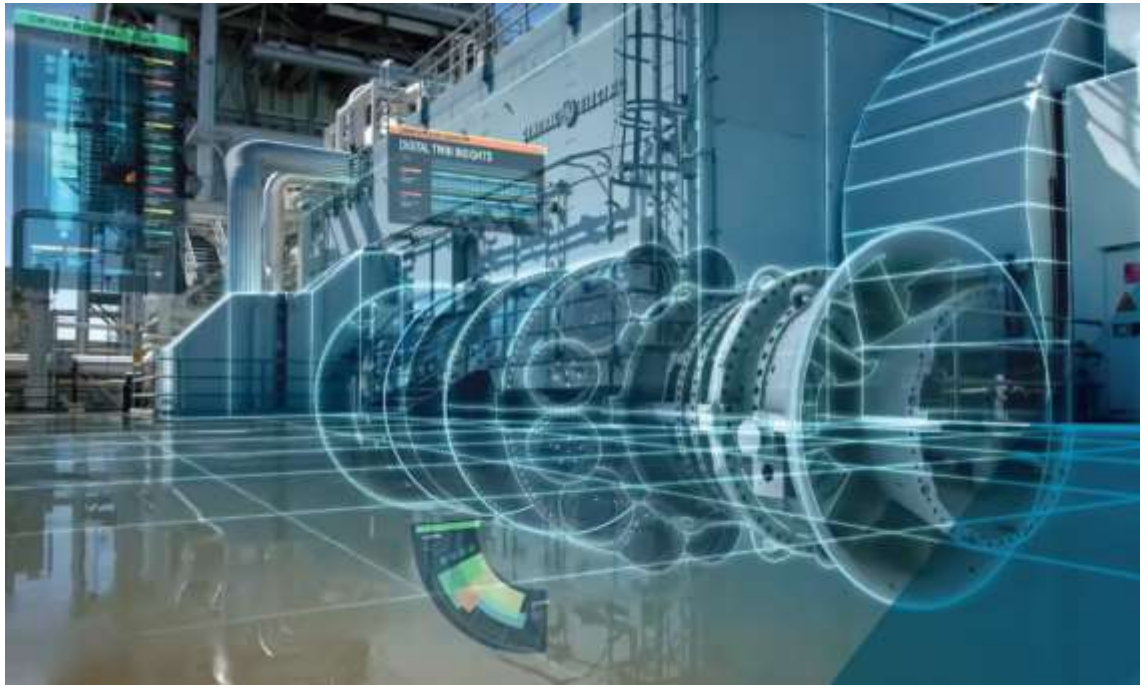
rbf™

In silico?

TOR VERGATA
UNIVERSITY OF ROME
Moving the boundaries of
in-silico cardiovascular analysis

Agenda

- Who are we?
  - rbfLAB @University of Rome Tor Vergata
  - RBF Morph
- An overview on Digital Twin
- Medical Digital Twin in EC funded Research
  - MeDiTATe
  - Copernicus
  - DiTAiD
- Advanced mesh morphing by RBF
- Parametric airways
- ROM and SSM
- Conclusions



Who are we? rbfLAB

- Department of Enterprise Engineering. Research team **rbfLAB,** Machine Design Group, involved in **national and international research projects**.

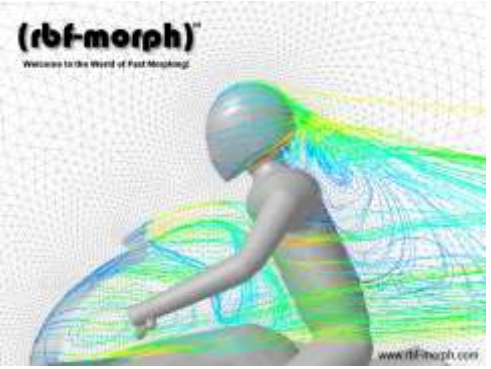
- https://www.rbflab.eu/
- rbfLAB focus is on:
  - Structural and fluid dynamic shape optimization (automotive, nautical, aerospace, biomedical).
  - Static and dynamic fluid structure interaction.
  - Advanced use of RBF (image analysis of deformations, flow fields interpolation).
  - Large-scale high-fidelity numerical simulations of flows in complex geometric configurations.
  - Reduced Order Models and Digital Twins.

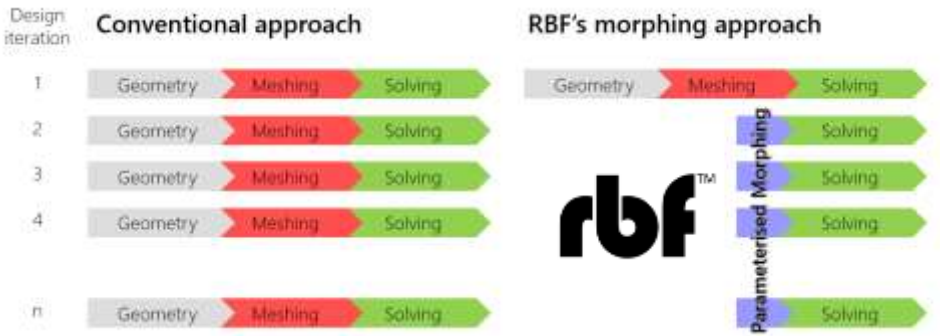
Who are we? RBF Morph

- RBF Morph is an ISV, **pioneer and world-leading provider** of numerical **morphing** techniques and CAE solutions. Inception in 2008 as on-demand solution for a Formula 1 top team
- **Start Up** founded at the beginning of 2016 to grow the business of the advanced mesh morphing software RBF Morph
- **Software line** composed by RBF Morph Fluids, Standalone RBF Morph, RBF Morph Structures.
- Technical Partner of ANSYS Inc. since 2009 (OEM since 2012)
- **Scale Up** stage expanding the market and the offe

http://www.rbf-morph.com/

- RBF Morph makes the CAE model **parametric**
- Shape parameters are driven by **an orchestrator**
- Shape parameters can be used to generate snapshots for real time Digital Twins (**ROM/AI**)





Who are we?

- **Partnership** between University of Rome "Tor Vergata" and RBF Morph: academic and industrial synergy
- Multi-sectoral CAE analysts, focused on high fidelity multi-physics problems
- Cutting edge technologies, academic research driven by industrial needs
- **Privileged position**: clear idea of the direction taken by industry, deep knowledge of the technologies available now and in the next future

Digital Twin **yesterday**-today-tomorrow

- Digital Twins are nothing new. Today we talk about DT a lot. But we have experience of DT daily use. ABS / ESP in our car. The Prius Hybrid (year 2004)!
- The governing equations of the physics of the twin were previously written by hand and then embedded in the electronics. Software components made up of great skills (for example vehicle dynamics). Telemetry and racing strategies in Formula 1. Advanced control systems on board the products.
- **Matlab Simulink**

Digital Twin yesterday-**today**-tomorrow

- System integration according to standards (an example are the FMU defined according to the FMI protocol *functional mockup interface*)
- Generic purpose IIoT platforms are available
- Twinning of industrial assets intended for the optimization of service, performance and maintenance
- **GE Predix**

"Digital twin eliminates the guesswork when determining the best way to service critical physical assets—from engines to power turbines. Easy access to this unique combination of deep knowledge and intelligence about your assets paves the road to optimization and business transformation."

Colin Parris, Vice President
GE Software Research

Digital Twin yesterday-today-**tomorrow**

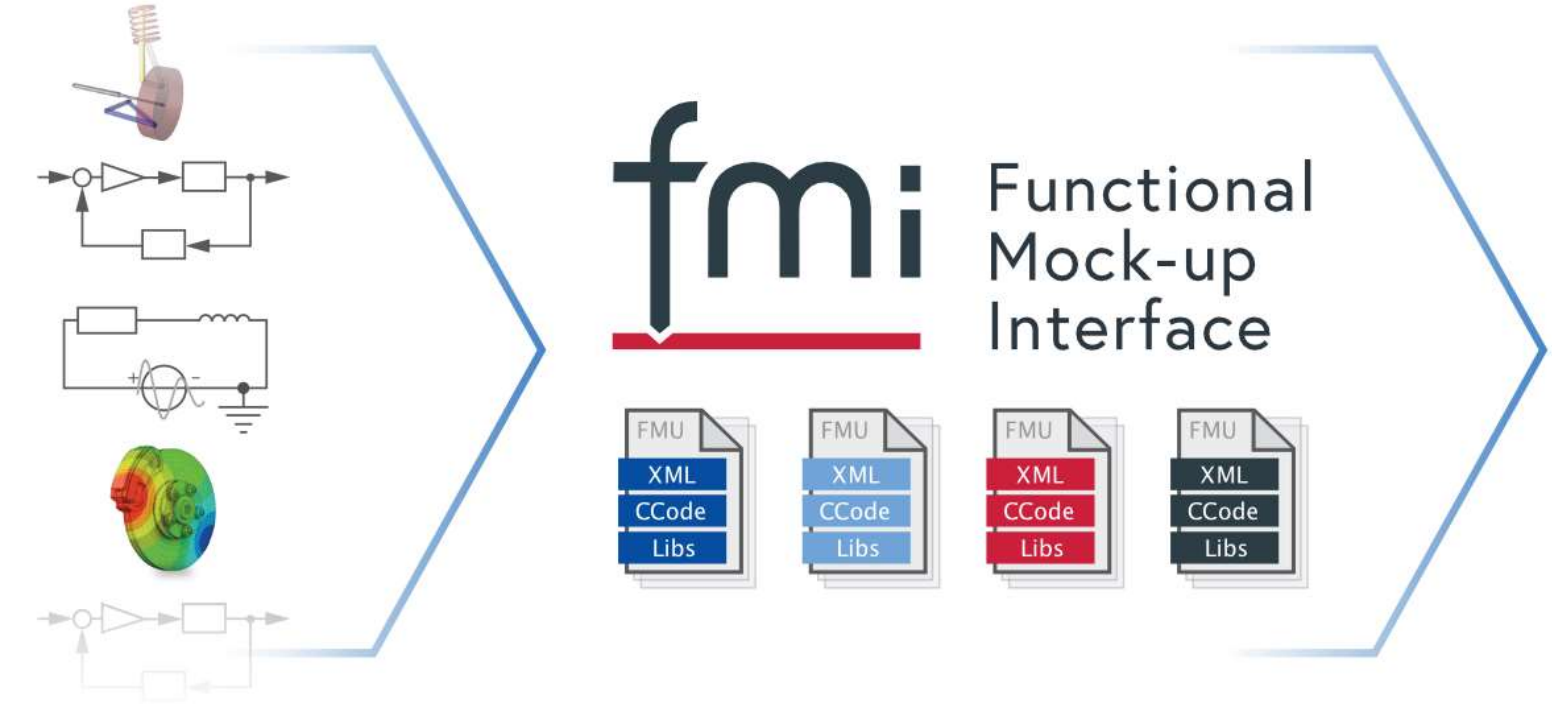
- Integration of high fidelity CAE (FEA, CFD, FSI) and system simulation ones (Modelica)
- Combination of AI, Machine Learning and numerical simulation (ROM)
- Hybrid twins combining historic Big Data (when available) with synthetic Big Data by simulation – data fusion
- **ANSYS Twin Builder**

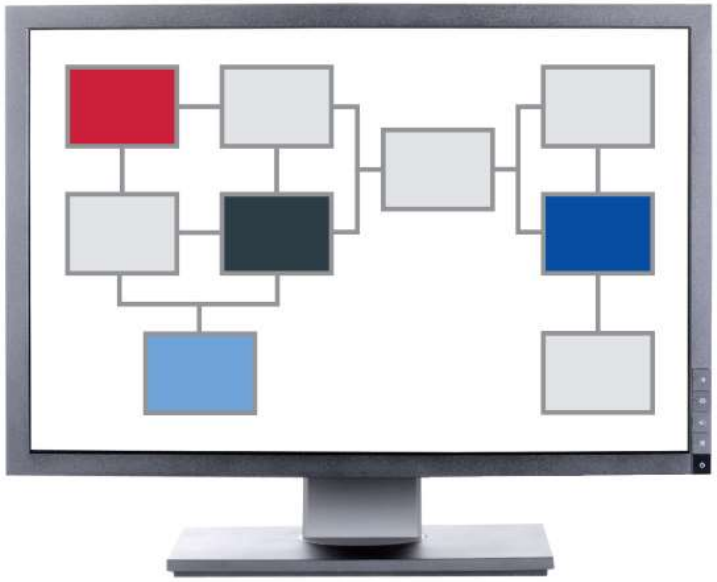
Digital Twin

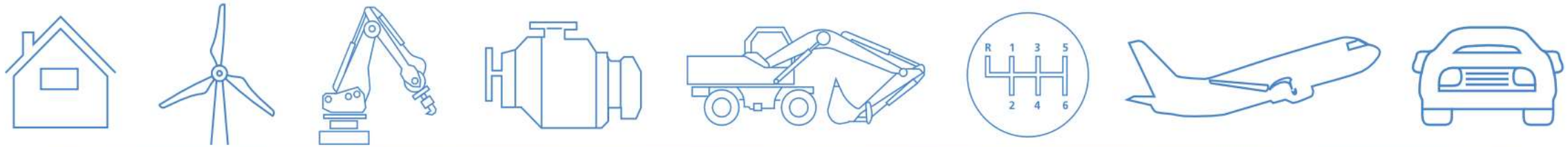
- A digital twin is a digital copy of an existing and working **physical asset**.
- It's connected with the actual state of the asset, remembers its history
- It allows to evaluate more about the current status of the asset. Can be used to forecast its evolution

Functional Mock-Up Interface

https://fmi-standard.org/







Digital Twin Consortium

digital twin CONSORTIUM

Founding Members

Ansys AUTODESK. Bentley DELL Technologies

GE Digital lendlease Microsoft NORTHROP GRUMMAN

https://www.digitaltwinconsortium.org/glossary/glossary.html

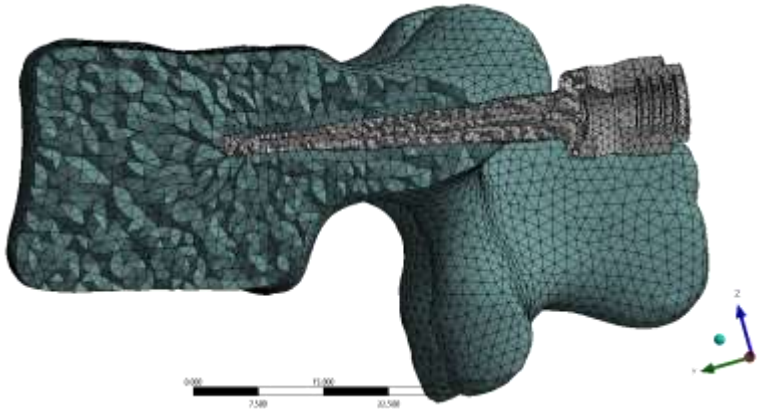
Medical Digital Twin

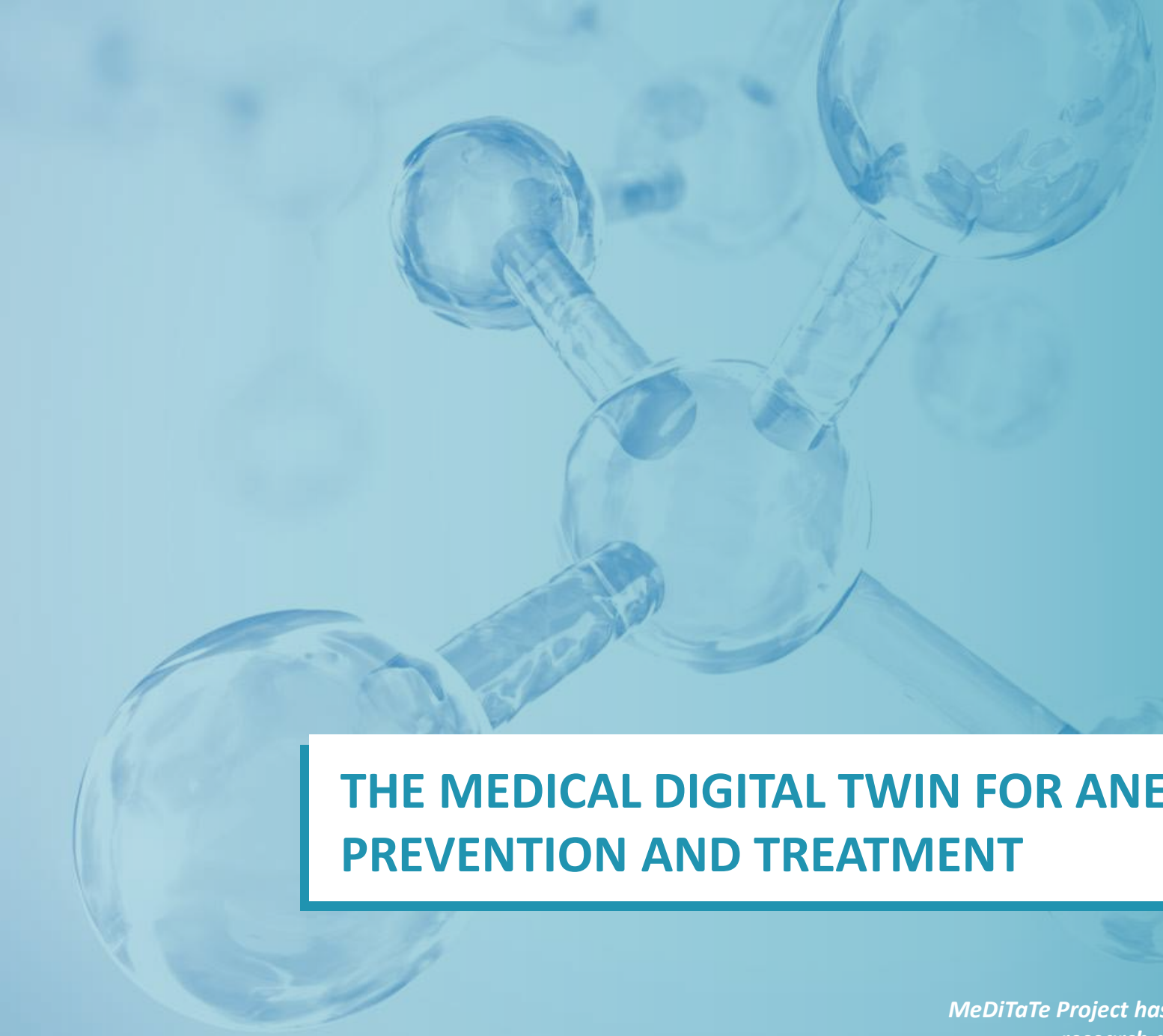
- Human body is a very important **physical asset**!
- Medical engineering combines **in silico** approach with the in vivo and in vitro ones
- CFD simulation of cardiovascular systems, structural simulations of stress acting on prostheses and on tissues, aerodynamic simulation of airways.
- Patient digital twin (Medical Digital Twin) aims at an easy adoption of in silico results in the medical environment (translation).
- Numerical simulation requires high performance computing (HPC) to have real time usage compression methods (ROM, PCA) are key enablers to adopt digital twin in real time
- Medical digital twin requires the fusion of image data and digital images (interactive visualization), the definition of biomarkers and the presentation of the results with tools and language that can be easily understood by the medical staff.
- https://www.avicenna-alliance.com/

Avicenna Alliance
Association for Predictive Medicine

Examples of Medical Digital Twin

- Aneurysms prevention and treatment (MeDiTATe project -The Medical Digital twin for aneurysm prevention and treatment)
- Shunting according to the mBTS (FF4EuroHPC project experiment - Cloud-Based HPC Platform to Support Systemic-Pulmonary Shunting Procedures)
- Patient specific airways treatment (FF4EuroHPC project experiment - Digital-Twin for Airflow and Drug Delivery in Human Airways)
- Patient specific spine surgery (Spinner Project - SPINe: Numerical and Experimental Repair strategies)



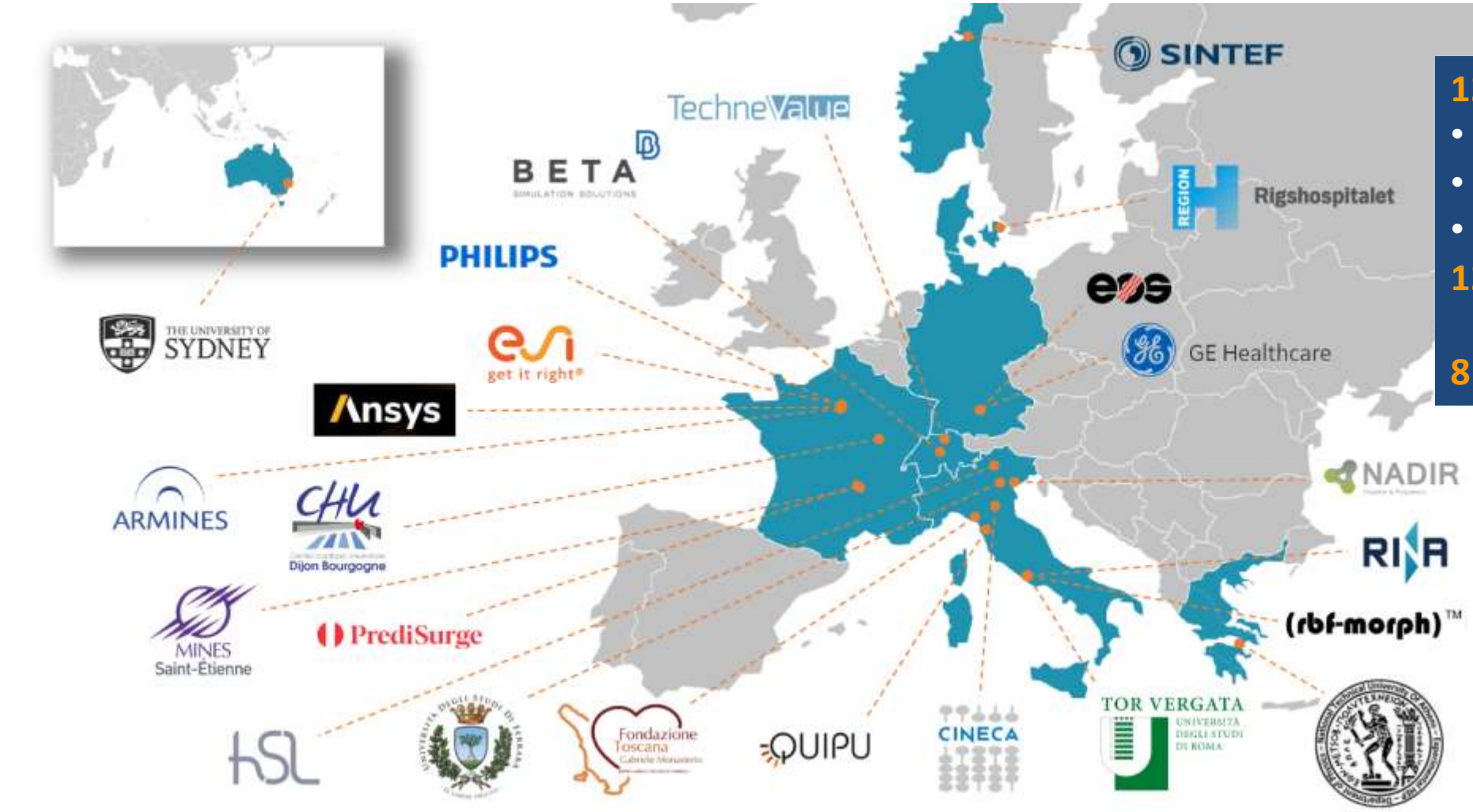


MEDITATE

THE MEDICAL DIGITAL TWIN FOR ANEURYSM PREVENTION AND TREATMENT

MeDiTaTe Project has received funding from the European Union's Horizon 2020 research and innovation programme under Grant Agreement 859836

Consortium



12 beneficiaries
- 3 academic
- 7 industrial
- 2 clinical centres

12 partners

8 countries

MEDITATE

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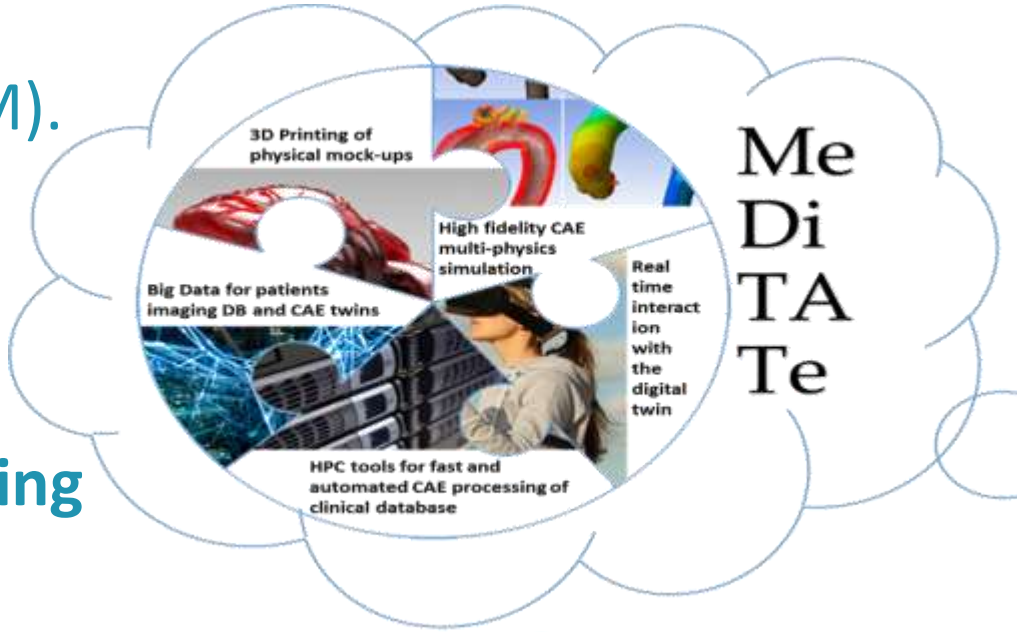
Research Tracks

1. High fidelity **CAE multi-physics** simulation with RBF mesh morphing (FEM, CFD, FSI, inverse FEM).
2. Real time interaction with the Digital Twin by **Augmented Reality**, Haptic Devices and **ROM**.
3. HPC tools, including GPUs, and cloud-based paradigms for **fast and automated CAE processing** of clinical databases.
4. Big Data management for population of patients imaging data and **high fidelity CAE twins**.
5. Additive Manufacturing of **physical mock-up** for surgical planning and training.



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Early Stage Researchers

https://meditate-project.eu/early-stage-reserachers/

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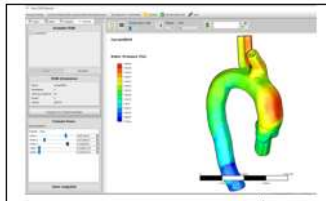
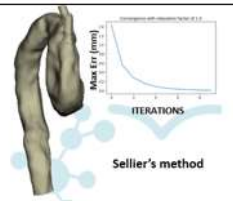
Individual Research Projects

https://meditate-project.eu/phd-projects/

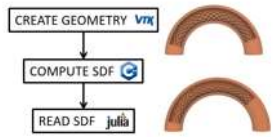


ESR1 Interactive ROM to reshape the aneurysm

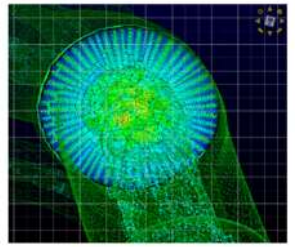


ESR2 Zero pressure shape definition for high fidelity FSI

MEDITATE



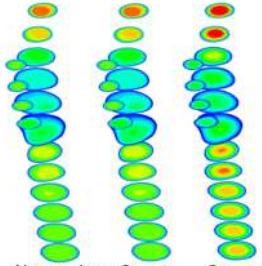
ESR3 Custom FEM beam solver for stent deploy



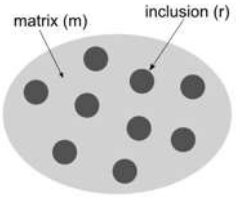
ESR4 Advanced meshing for accurate HiFi GPU simulations

PUMA (NTUA)

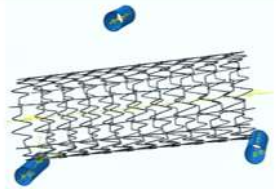
ESR5 FSI coupling simulation accelerated with GPU



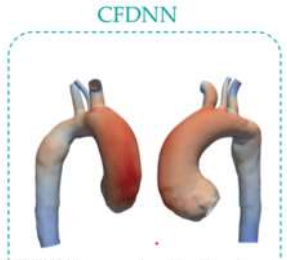
ESR6 Non-Newtonian fluids modelling



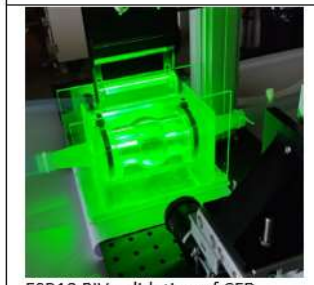
ESR7 Material models matched by FEA identification of image data



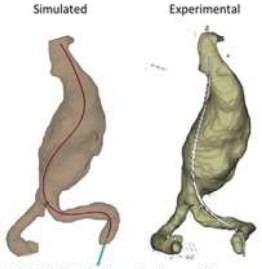
ESR8 Auxetic structures are modelled by nonlinear FEA



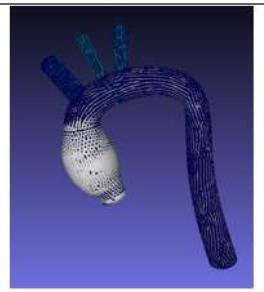
ESR9 CFD computed by Physics informed Machine Learning



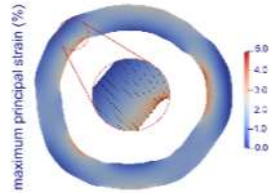
ESR10 PIV validation of CFD simulations of phantoms



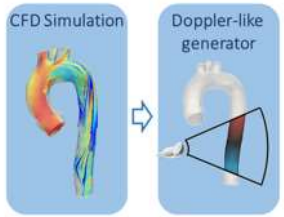
ESR11 FEM simulation of guided navigation



ESR12 RBF Mesh Morphing of patient specific vessels



ESR13 RBF predicted strain map on US images



ESR14 CFD digital twin to simulate US

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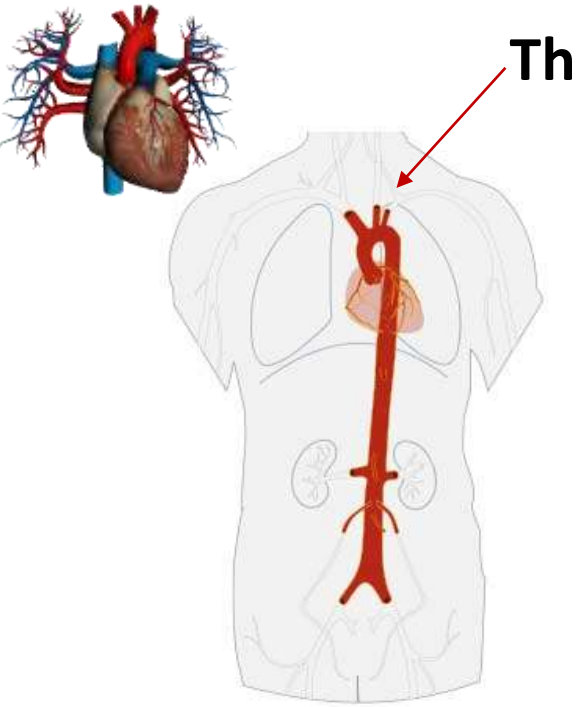
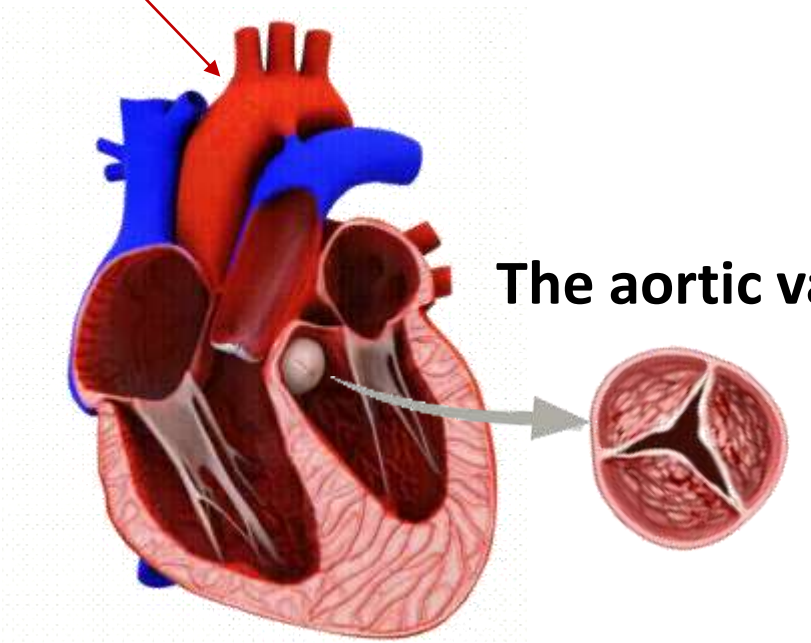
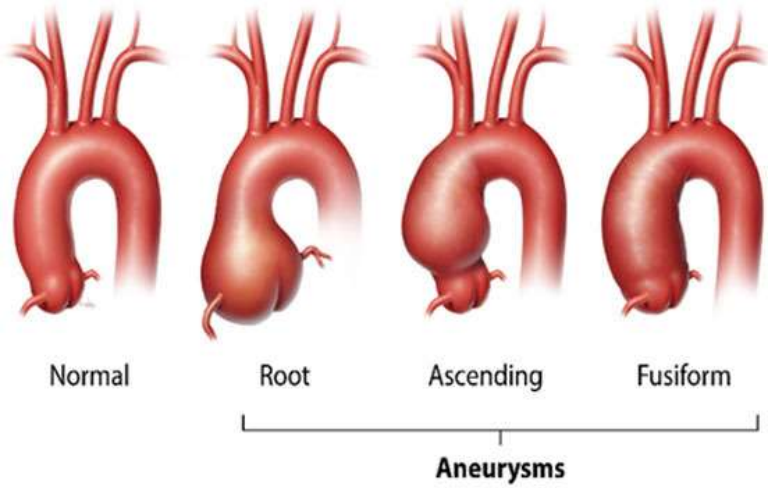
The Anatomy and the Clinical Problem







The **criterion** to perform **ascending aortic aneurysm surgery** is currently based only on the evaluation of the ascending aorta **diameter**.

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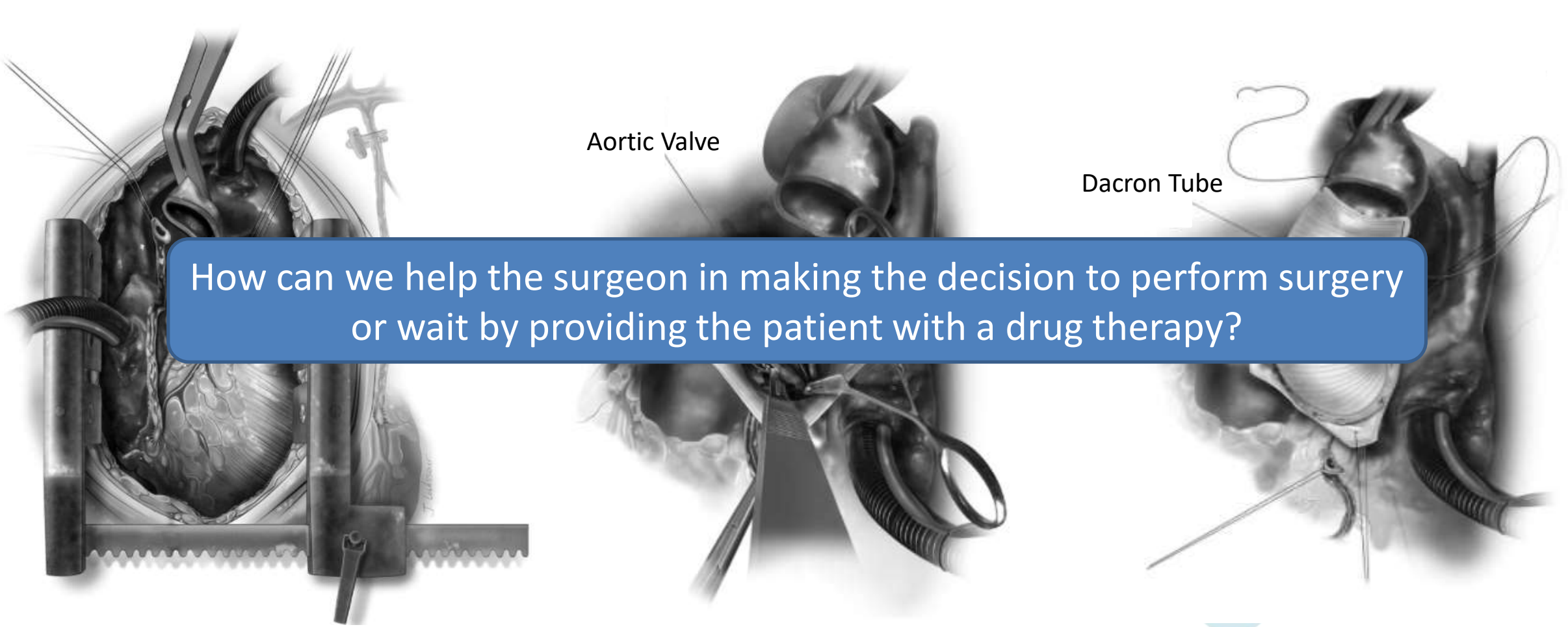
The surgery



How can we help the surgeon in making the decision to perform surgery or wait by providing the patient with a drug therapy?

[1] Leonard N.Girardi, MD, Operative Techniques in Thoracic and Cardiovascular Surgery

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Digital Twin and Real Time Simulation

Creating a workflow to go from images to simulation results in a few seconds

Rapid growth

ANEURYSM GROWTH RATE

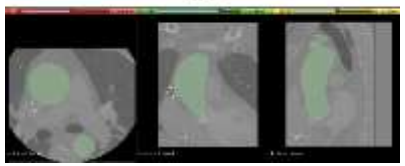
No growth

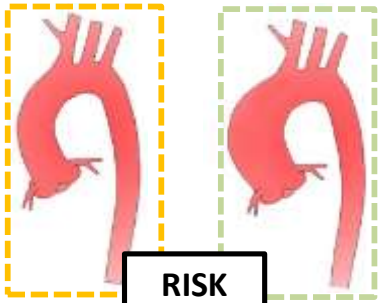
SEMI-AUTOMATIC SEGMENTATION

METRICS ON THE GEOMETRY

STATISTICAL SHAPE MODELING

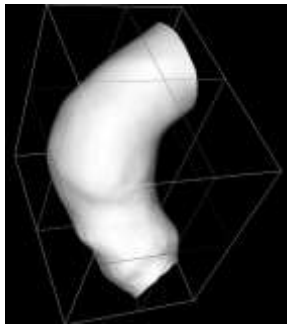
3DSlicer



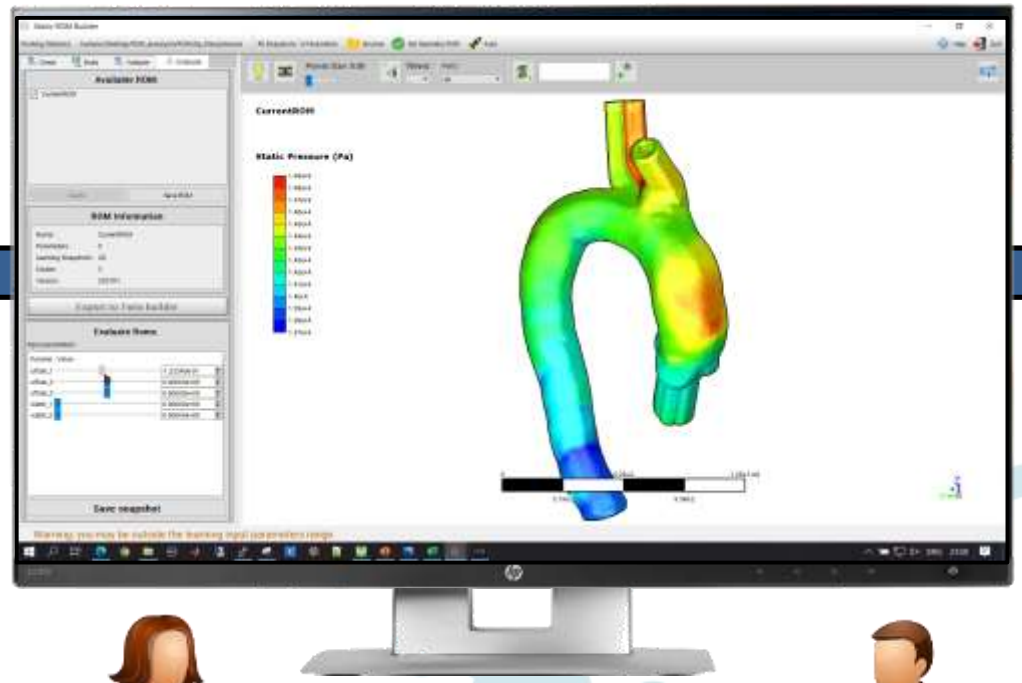


RISK

LOW HIGH



REDUCED ORDER MODELS AND REAL-TIME SIMULATION



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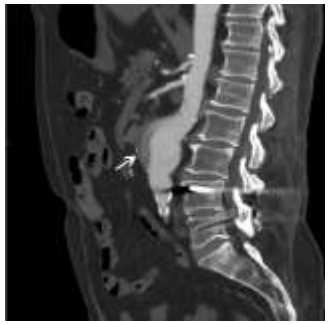
Endovascular Abdominal Aneurysm Repair

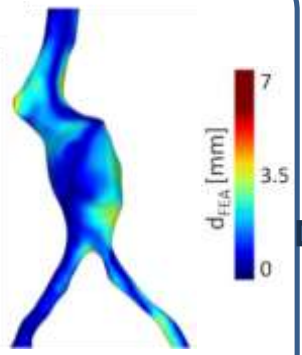
AAA patient case

ST. OLAVS HOSPITAL
UNIVERSITETSSYKEHUSET I TRONDHEIM



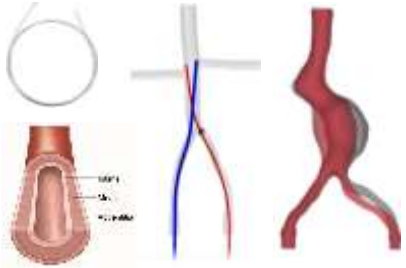
CT scan segmentation

3DSlicer



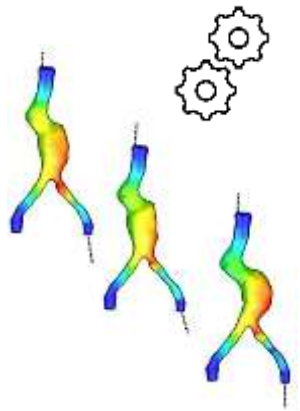
Baseline Finite Element case

Ansys
LS - DYNA



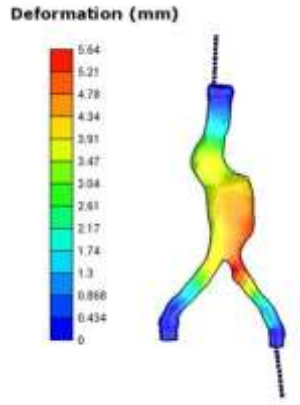
Morphological, clinical, mechanical parameterization

rbf™
python™



ROM Build-up

Ansys
TWIN BUILDER



ROM exploitation

Ansys
TWIN BUILDER

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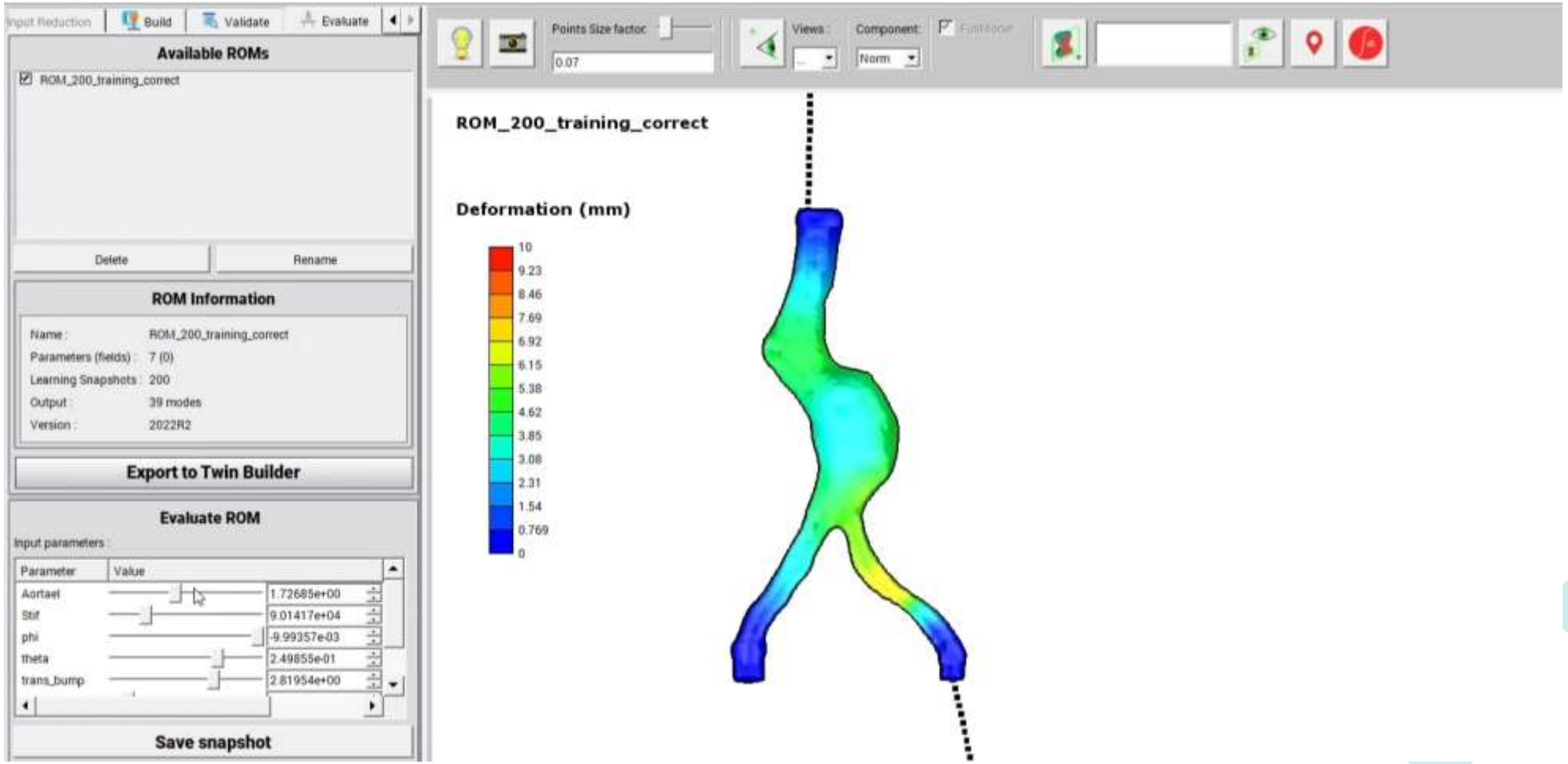
Endovascular Abdominal Aneurysm Repair



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FF4EuroHPC

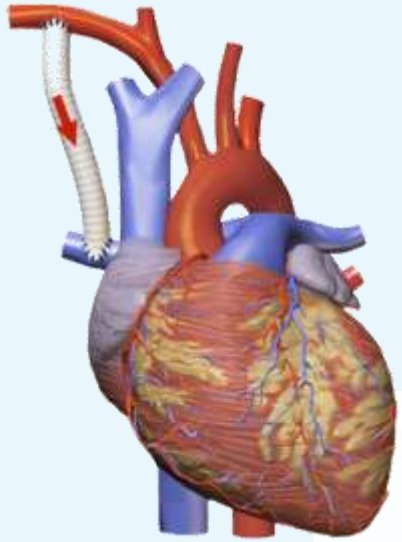
Copernicus

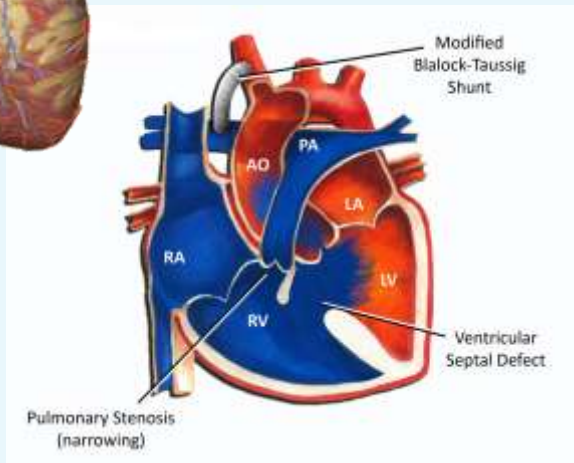
Cloud-based HPC platform to support systemic-pulmonary shunting procedures

This project has received funding from the European High-Performance Computing Joint Undertaking Joint Undertaking (JU) under grant agreement No 951745. The JU receives support from the European Union's Horizon 2020 research and innovation programme and Germany, Italy, Slovenia, France, Spain.

The Problem

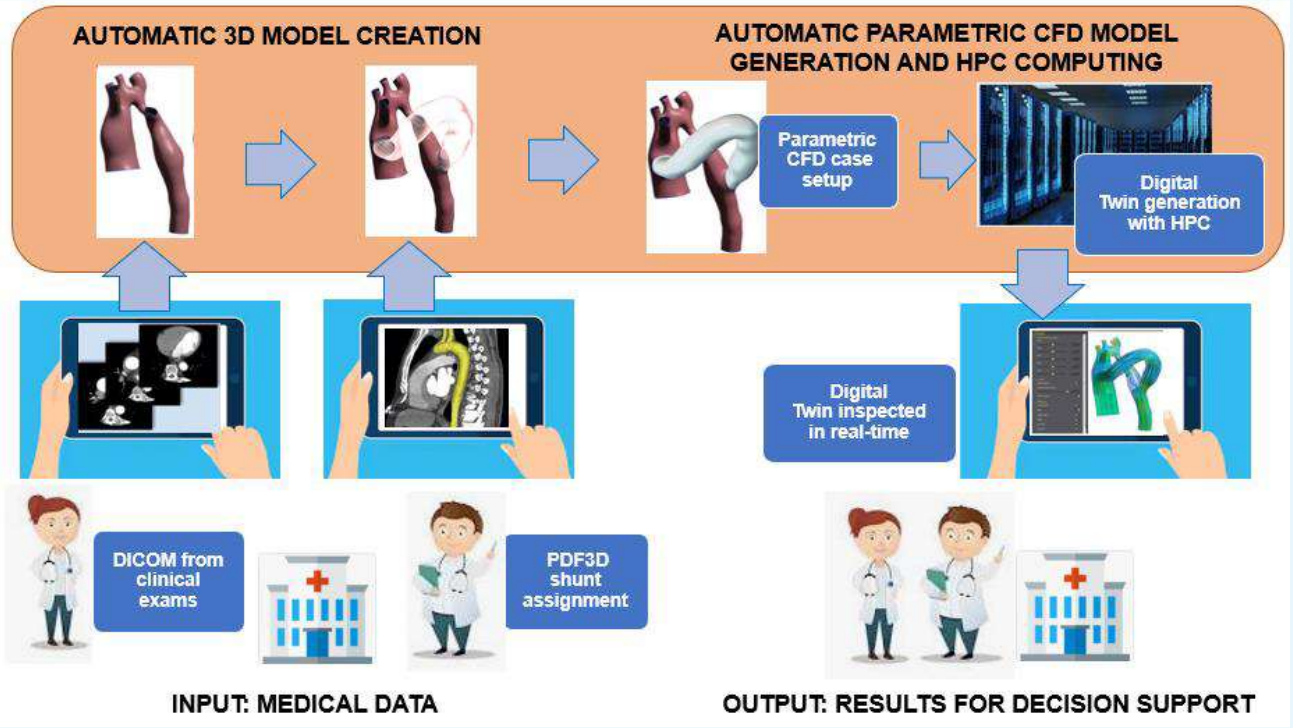
- **Congenital heart diseases** (CHDs) account for nearly **one-third** of all congenital birth defects and **7th cause of death** in children younger than 1 year in 2017.
- Without the ability to alter the prevalence of CHD, interventions and resources must be focused to **improve survival** and **quality of life**.
- The **Modified Blalock Taussig Shunt** (mBTS) is a common **palliative operation** on cyanotic heart diseases, but it is associated with **significant mortality** (~7,2%).



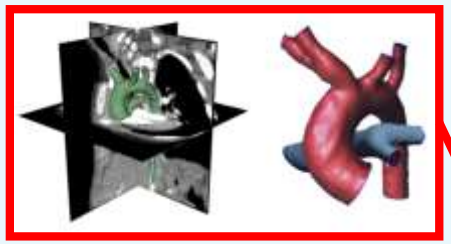


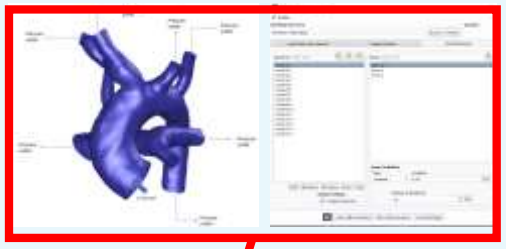
Experiment Approach & Expected Outcome

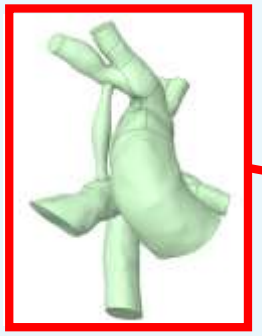
- The Copernicus application aims to provide an interactive **Medical Digital Twin** (MDT) of the patient-specific district to **support the surgery planning of mBTS under critical conditions**.
- The procedure was designed considering **advanced numerical means** with the objective to deploy MDT within ~**48hh**.



Proposed solution







CT Image Segmentation (Python Code)

CAD Reconstruction + Shunt creation (SpaceClaim)

Surface and volume Mesh generation (Fluent – Watertight)

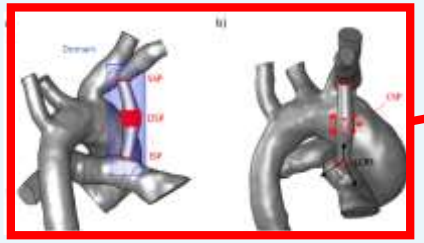
CFD and Snapshot set-up (Fluent – RBP)

RBF Shape modifiers set-up (Fluent – RBF Morph)

HPC for Snapshot generation (Fluent – RBF Morph

ROM Generation (Twin Builder)

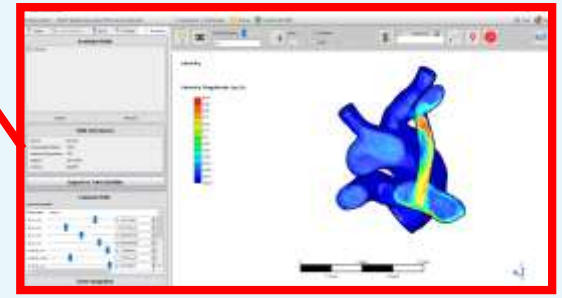
ROM Evaluation (Twin Builder)



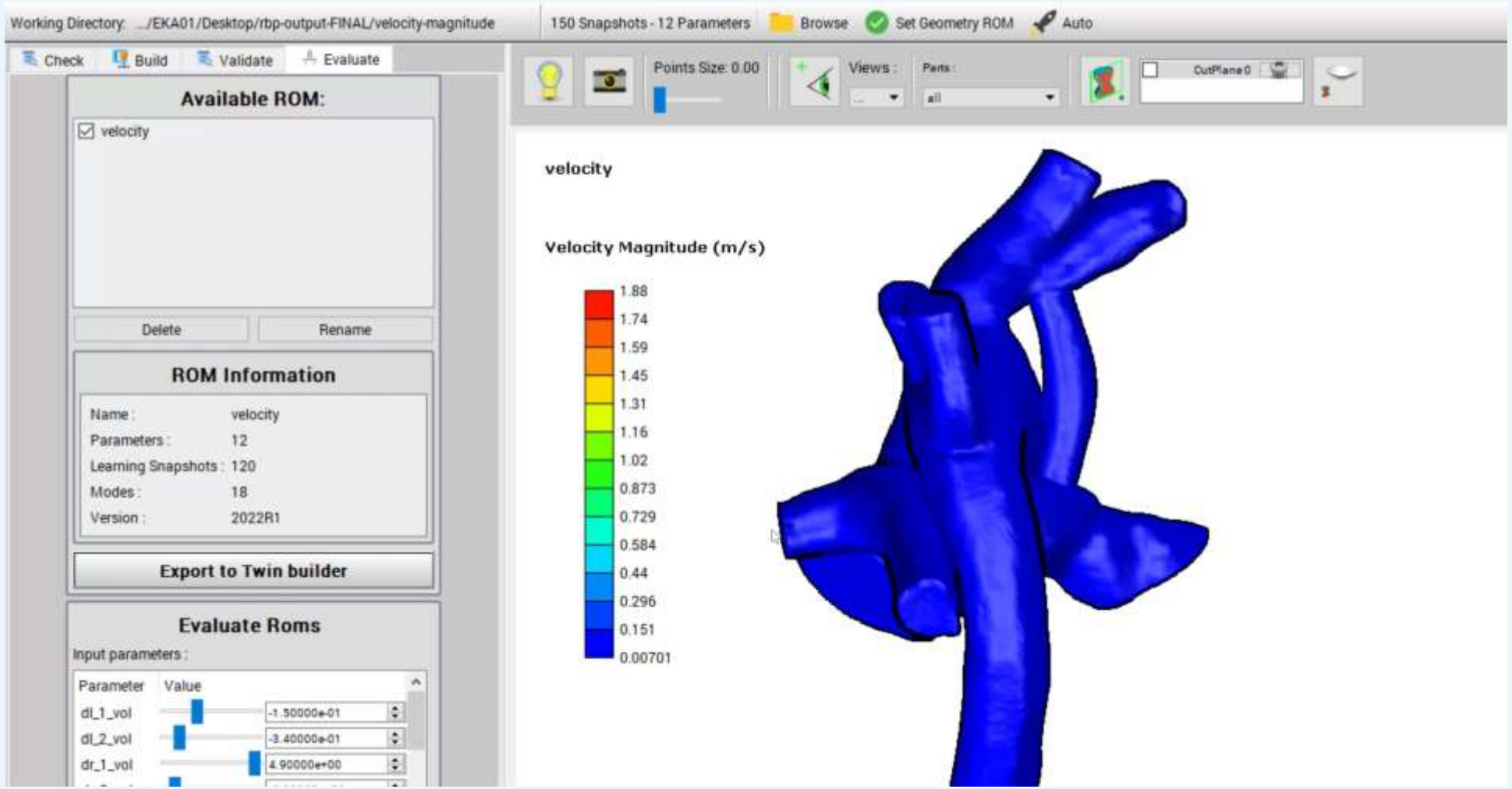
Copernicus Pre-Processing

Copernicus Computing

Copernicus Post-Processing



Proposed solution



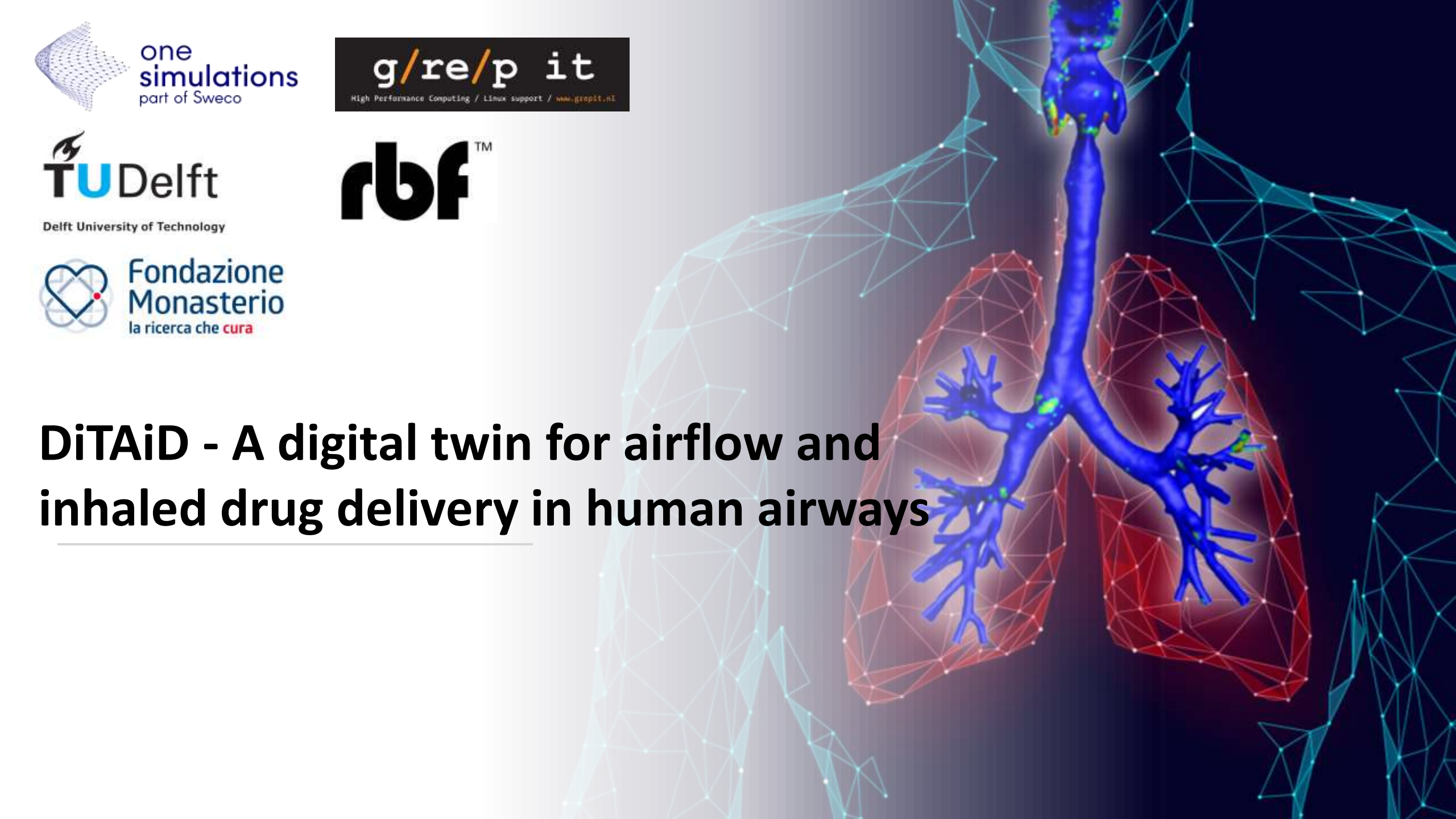
one simulations
part of Sweco

g/re/p it
High Performance Computing / Linux support / www.grepit.nl

TU Delft
Delft University of Technology

rbf™

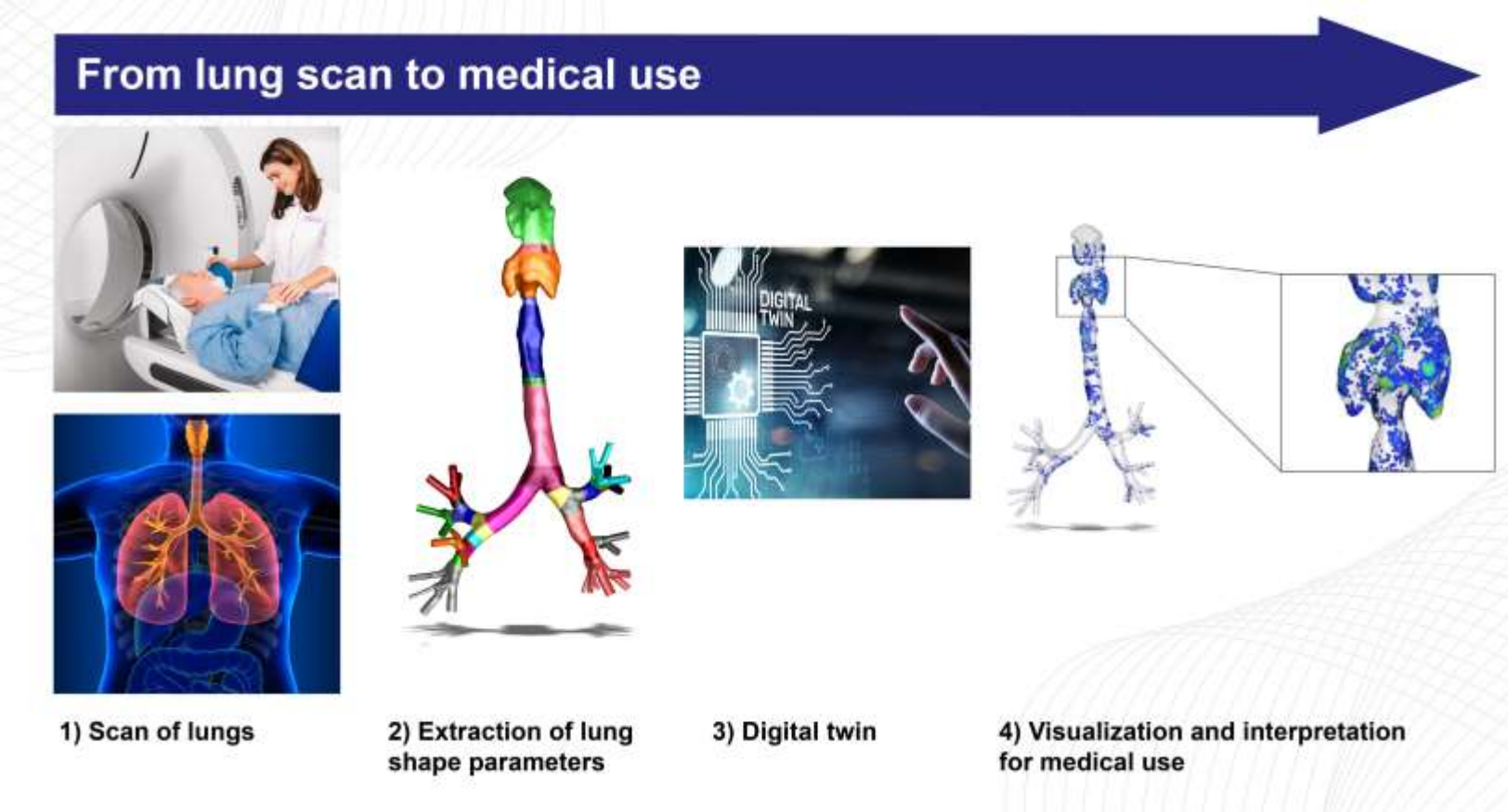
Fondazione Monasterio
la ricerca che cura



DiTAiD - A digital twin for airflow and inhaled drug delivery in human airways

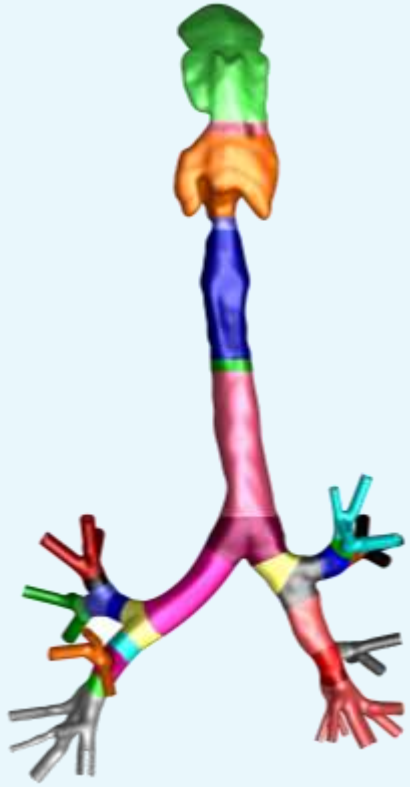
The digital twin

- **The developed digital twin can:**
  - ✓ Provide similar results compared to CFD simulations
  - ✓ Keeping a good level of detail
  - ✓ Provide patient specific results within minutes compared to weeks
- **The digital twin is created by combining a large number of CFD simulations (snapshots) using Reduced Order Modelling (ROM) techniques**



Lung geometry definition

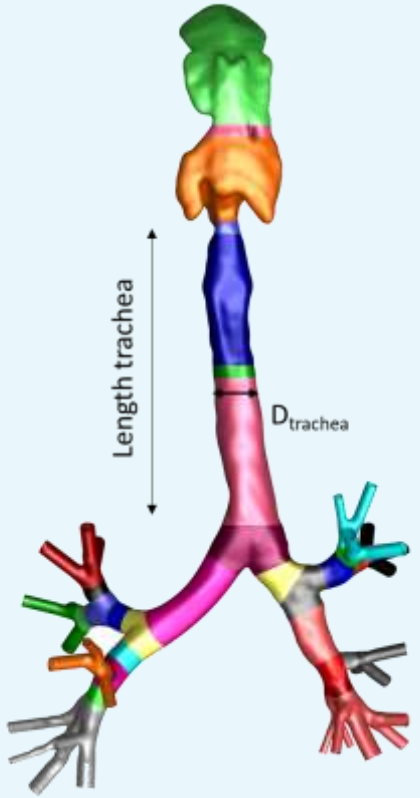
- **Base geometry is obtained from literature**
  - ✓ Constructed from several high-resolution CT scans of 47 year old healthy volunteer
  - ✓ The base geometry has been studied in multiple experimental and numerical studies
  - ✓ Includes up to the 4th generation (note, human lungs go up to 23 generations)
- **Identify relevant input parameters for the digital twin**
  - ✓ Shape
  - ✓ Flow
  - ✓ Particle



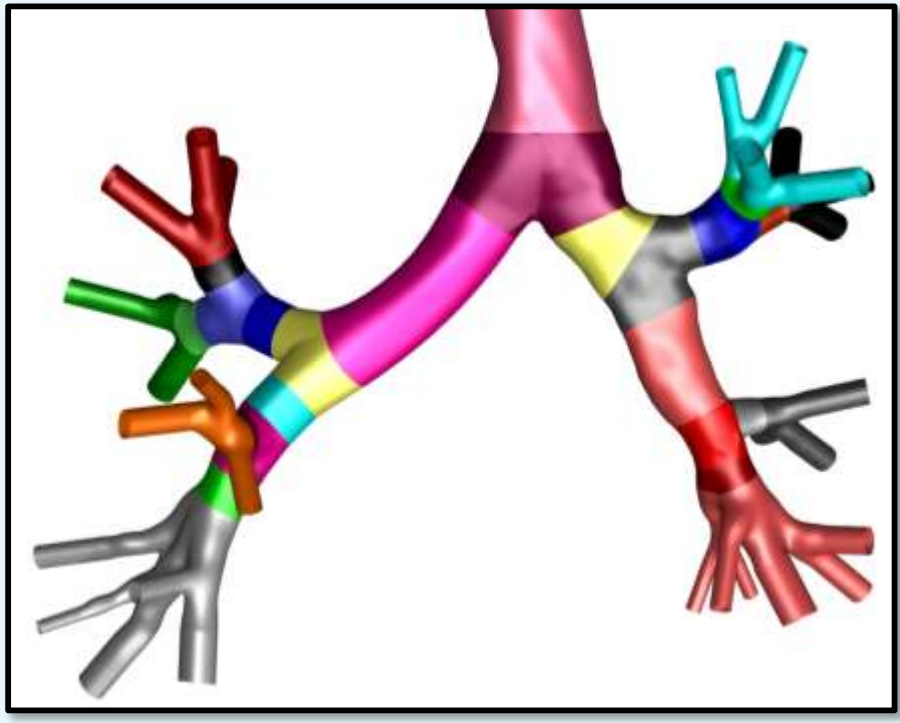
Z. Zhang, C. Kleinstreuer and S. Hyun, "Size-change and deposition of conventional and composite cigarette smoke particles during inhalation in a subject-specific airway model," *Journal of Aerosal Science*, vol. 46, pp. 34-52, 2012.
S. Kenjereš and J. L. Tjin, "Numerical simulations of targeted delivery of magnetic drug aerosols in the human upper and central respiratory system: a validation study," *Royal Society Open Science*, vol. 4, no. 12, p. 170873, 2017.

Identify shape parameters

- **Potentially a huge amount of shape parameters!**
- **Amount of input parameters is limited by assuming:**
  - ✓ **Circularity is kept constant**
  - ✓ **Only considered angle is the branching angle**
  - ✓ **Diameter follows a fixed ratio6 of h=0.79**
- **Mouth-throat part: 3 parameters**
- **Lower airways: 23 parameters**
  - ✓ **Generation 0 (trachea): 1L, 1D, 1A**
  - ✓ **Generation 1: 2L, 2A**
  - ✓ **Generation 2: 4L, 4A**
  - ✓ **Generation 3: 8L**



T. Van de Moortele et al.; *"Morphological and functional properties of the conducting human airways investigated by in vivo computed tomography and in vitro MRI"*



Generation	Diameter [mm]	Length [mm] Left	Length [mm] Right	Branching angle [deg]
0 (Trachea)	15 - 20	100 - 120		80 - 95
1		51 - 57	24 - 28	75 - 90
2		12 - 16	15 - 28	65 - 95
3		7 - 10	7 - 10	55 - 70

Identify flow & particle parameters

https://www.flickr.com/photos/aceofknaves/25604600281/

Physical parameters: 3 parameter

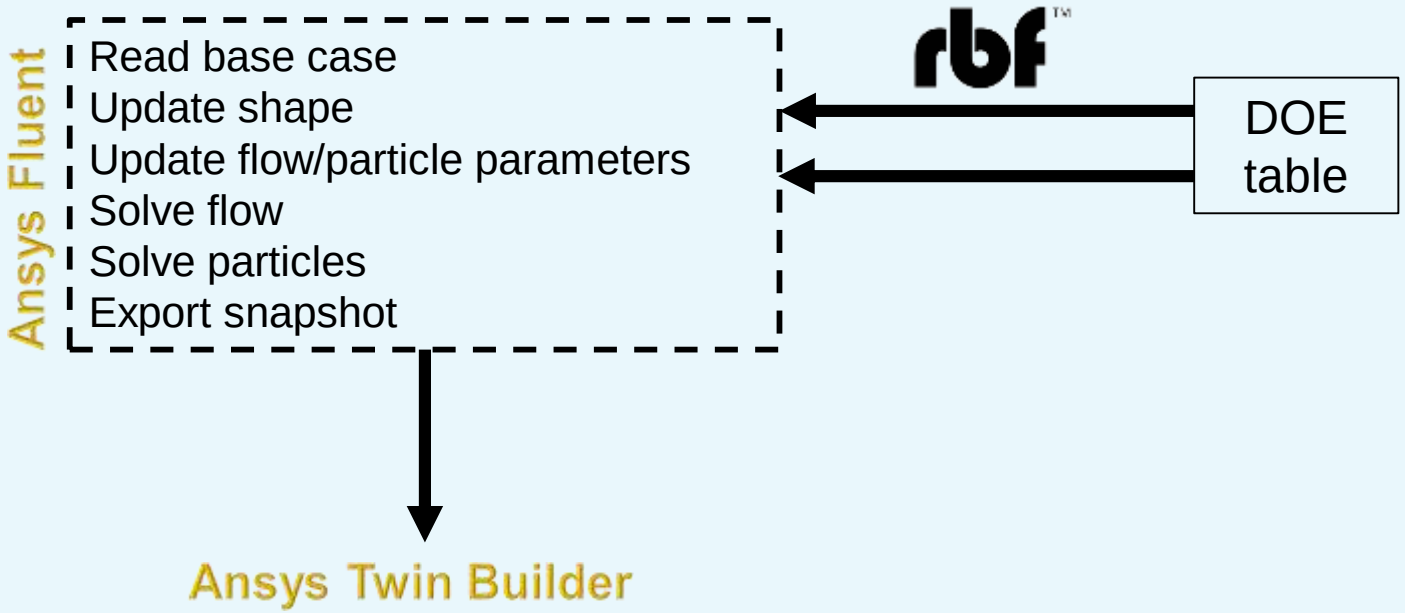
- ✓ Flow rate varies between 15 L/min and 120 L/min
- ✓ Particle size varies between 0.1 µm and 10 µm
- ✓ Particle injection rate varies between 0 m/s and 10 m/s

26 shape parameters and 3 physical parameter

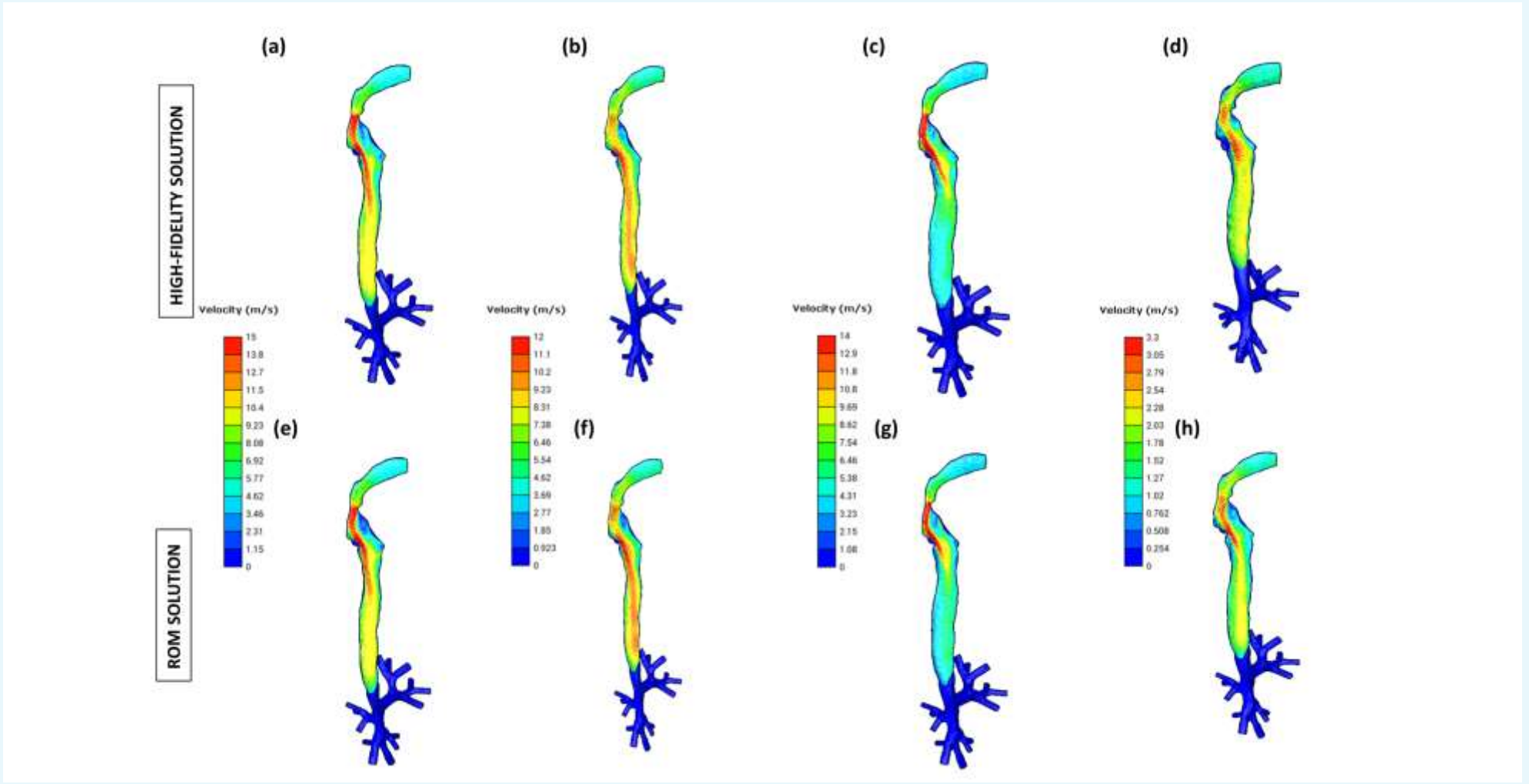
29 input parameters in total

Parametric study

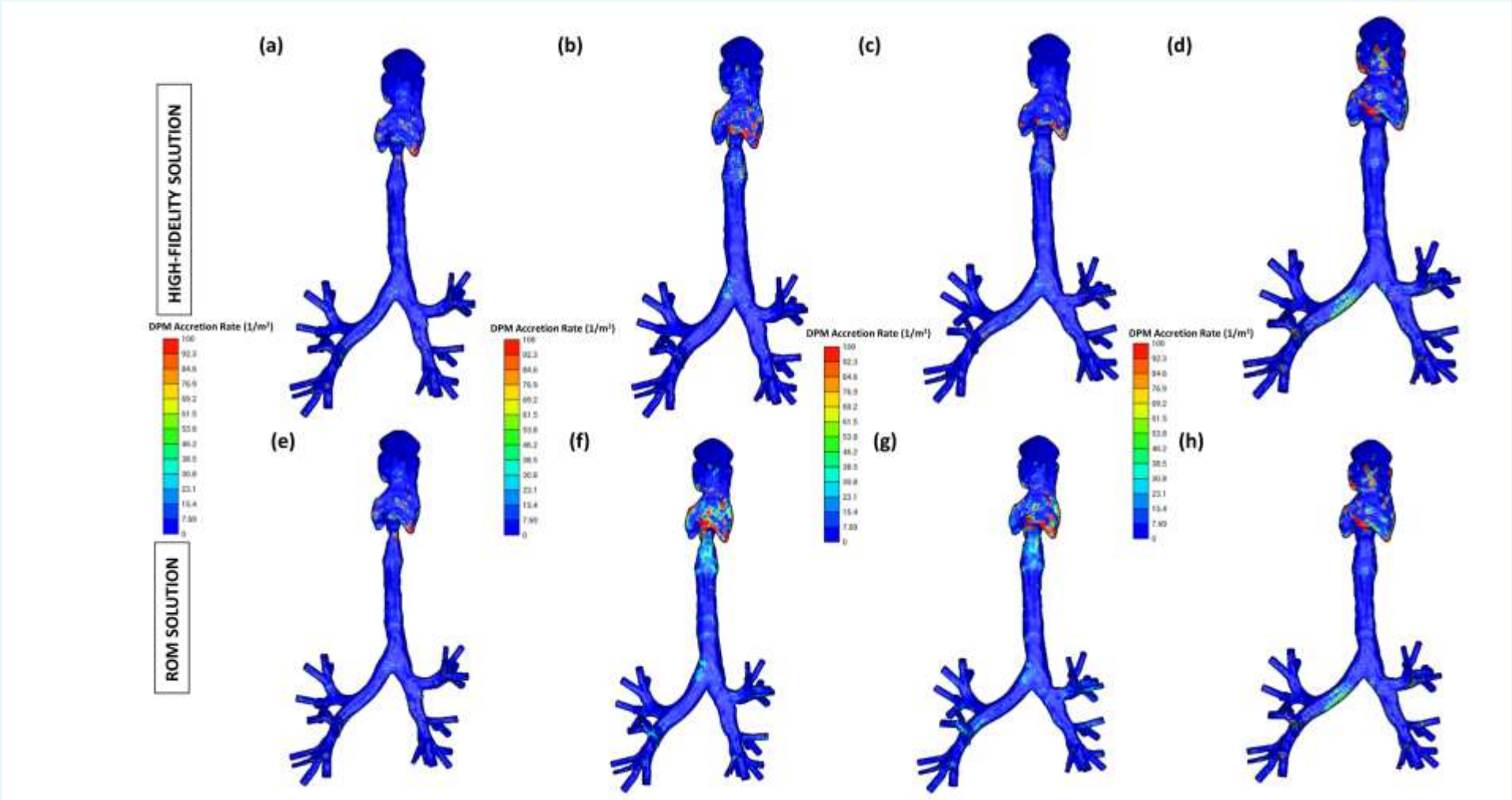
- **Design Of Experiments (DOE) table is generated:**
  - ✓For the 29 input parameters
  - ✓Using the Latin Hypercube Sampling for optimal spacing
  - ✓Creating 1000 design points
- **Fluent settings validated in literature**
  - ✓Steady state
  - ✓RANS, transitional SST (4eq)
  - ✓Particles are one-way coupled



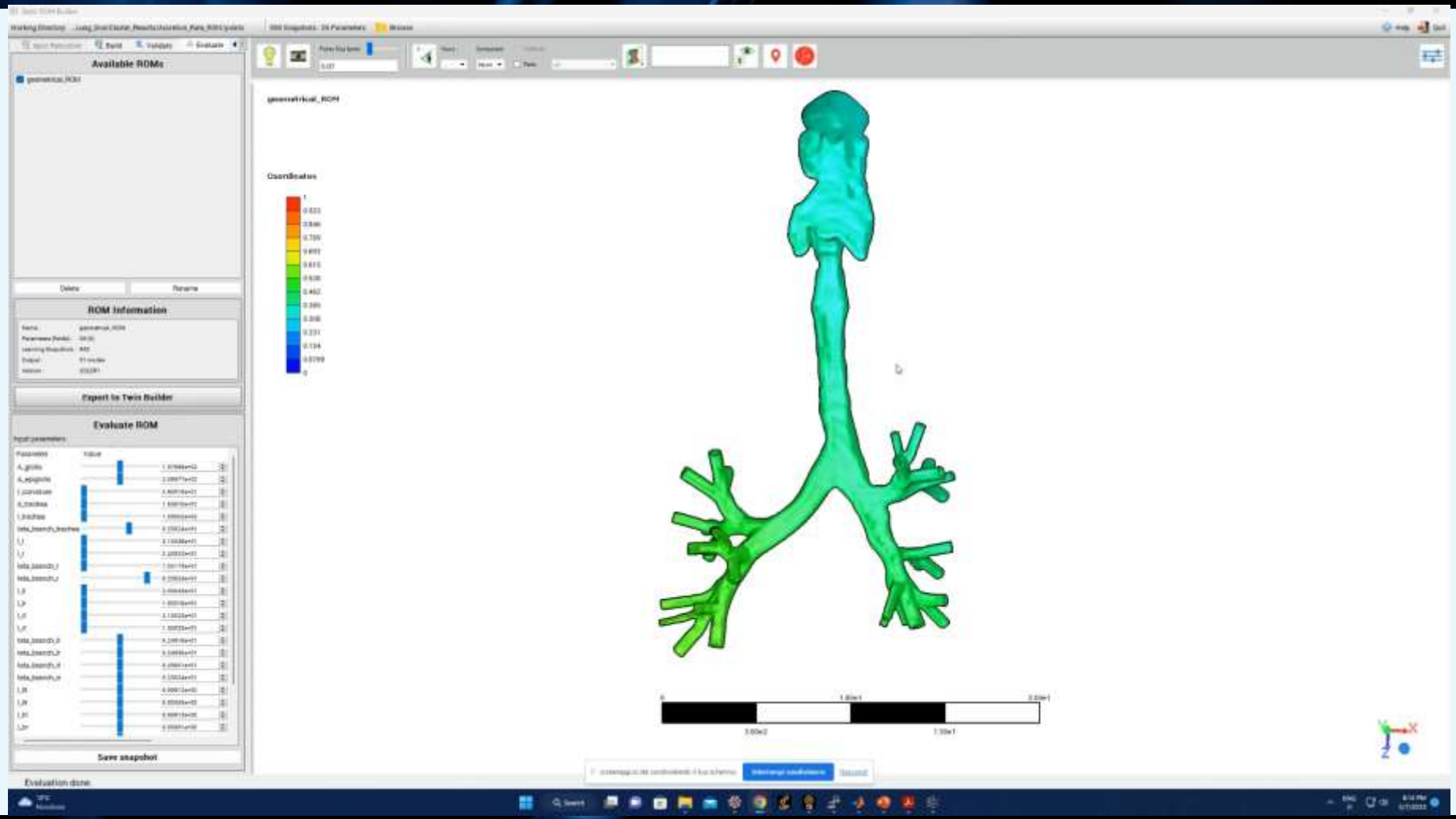
Results: Velocity



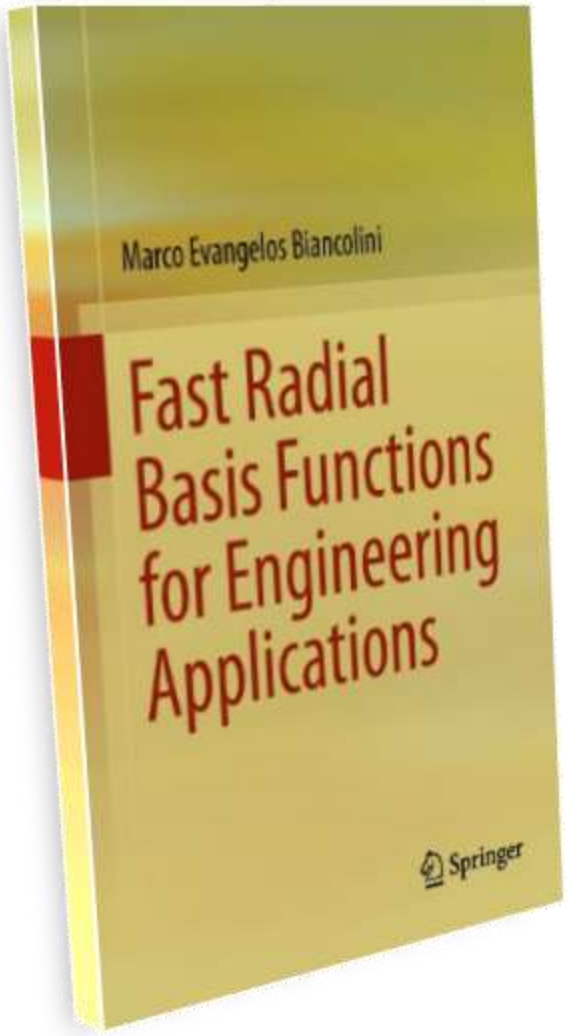
Results: Particle deposition



Results: interactive model



Radial Basis Functions background



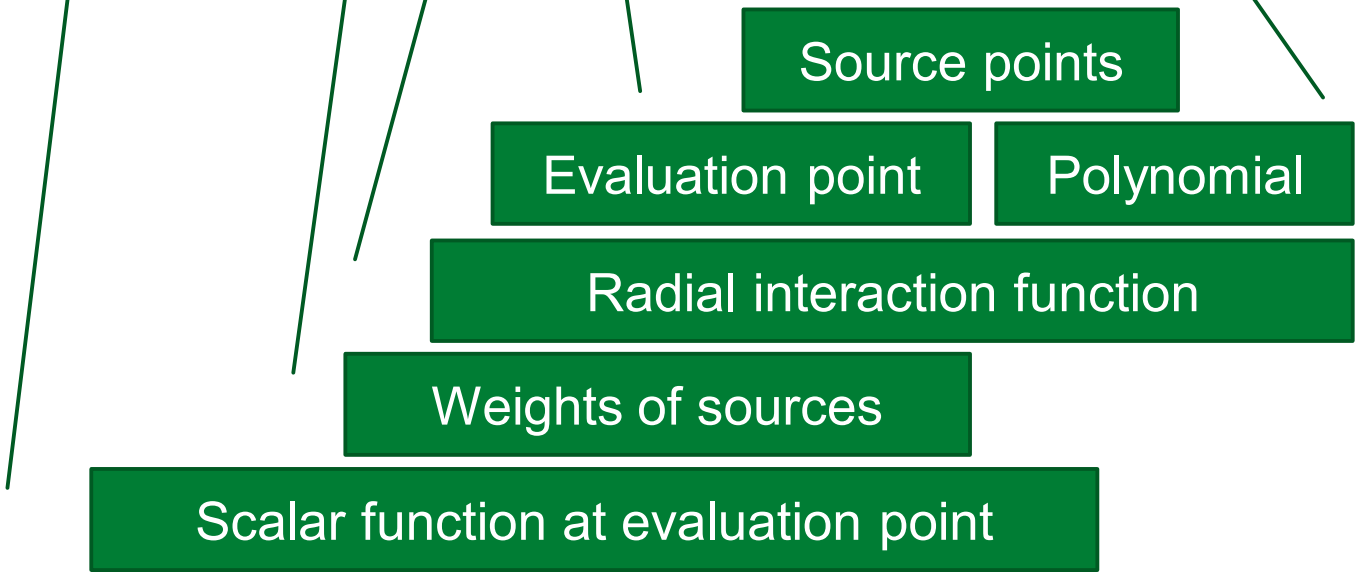
$$s(\boldsymbol{x}) = \sum_{i=1}^{N} \gamma_i \cdot \varphi\left(\left\|\boldsymbol{x} - \boldsymbol{x}_{\boldsymbol{k}_i}\right\|\right) + h(\boldsymbol{x})$$

- Source points
- Evaluation point
- Polynomial
- Radial interaction function
- Weights of sources
- Scalar function at evaluation point

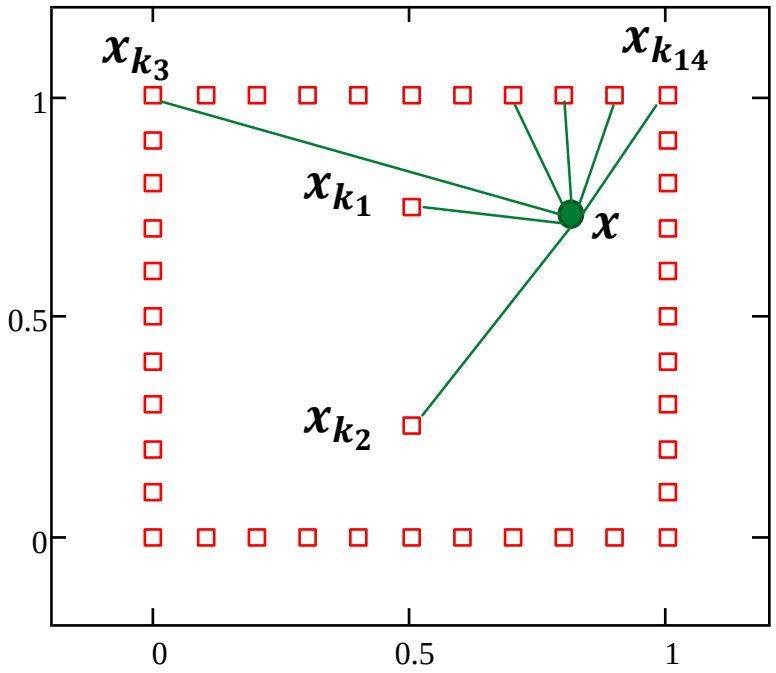
Radial Basis Functions background

- **Radial Basis Functions** (RBF) were introduced as interpolators of scattered data in sixties. Usually the interpolation is comprised of:
  - A sum of weighted radial interactions
  - A polynomial correction
- RBF are commonly used to interpolate a **scalar function** defined in a multi-dimensional space ($\mathbb{R}^n \rightarrow \mathbb{R}$)

$$s(\boldsymbol{x}) = \sum_{i=1}^{N} \gamma_i \cdot \varphi\left(\left\|\boldsymbol{x} - \boldsymbol{x_{k_i}}\right\|\right) + h(\boldsymbol{x})$$



Radial Basis Functions background



$$s(\boldsymbol{x}) = \sum_{i=1}^{N} \gamma_i \cdot \varphi\left(\left\|\boldsymbol{x} - \boldsymbol{x}_{\boldsymbol{k_i}}\right\|\right) + h(\boldsymbol{x})$$

Source points

Evaluation point

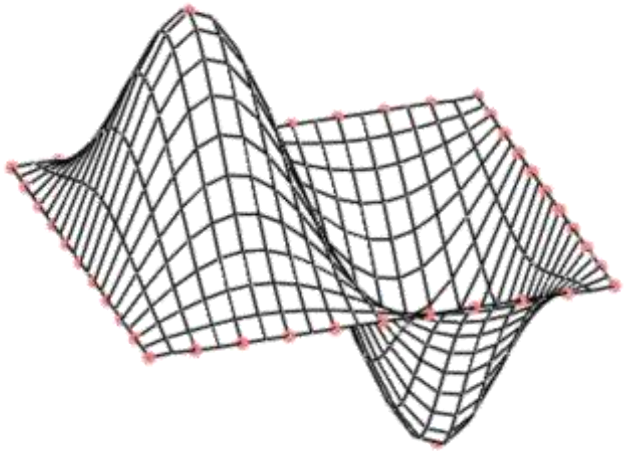
Polynomial

Radial interaction function

Weights of sources

Scalar function at evaluation point

Radial Basis Functions background

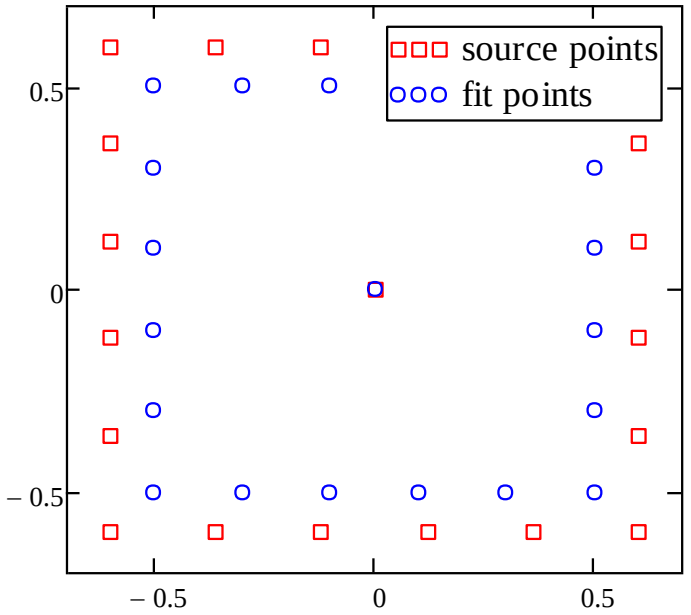


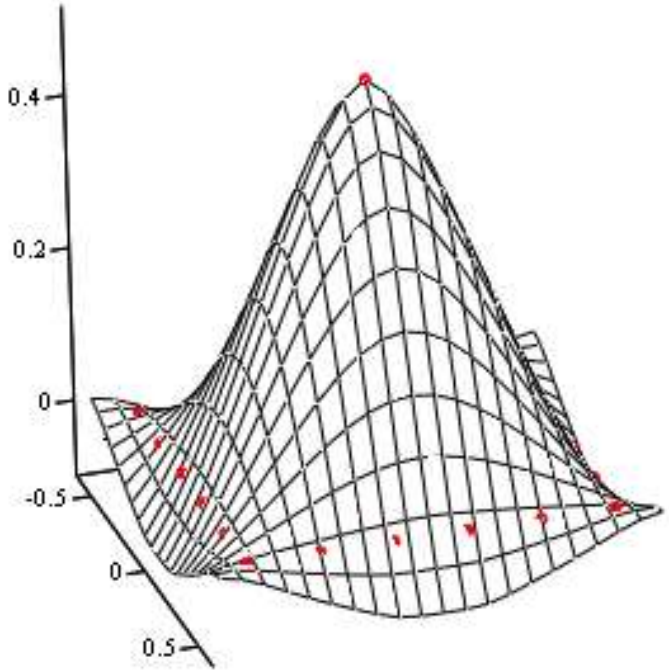
$$s(\boldsymbol{x}) = \sum_{i=1}^{N} \gamma_i \cdot \varphi\left(\left\|\boldsymbol{x} - \boldsymbol{x_{k_i}}\right\|\right) + h(\boldsymbol{x})$$

- Source points
- Evaluation point
- Polynomial
- Radial interaction function
- Weights of sources
- Scalar function at evaluation point

Radial Basis Functions background

- The **weights of the RBF** are computed using regression/interpolation:
  - From scalar values at source points
  - From scalar values at fit points
- RBF fit (known as RBF training):
  - Solving a linear system (interpolation)
  - Using Least Squares



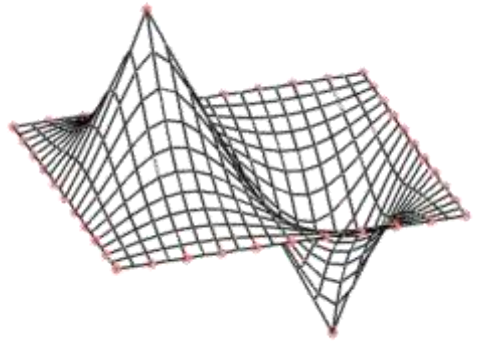


Radial Basis Functions background

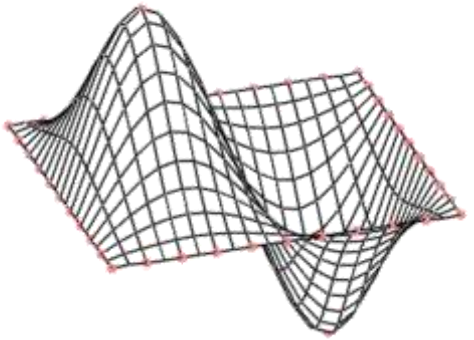
- RBF with **global support**
  - Far field interactions
  - Dense system of equations to be solved
- RBF with **compact support**
  - Local interactions
  - Sparse systems of equations to be solved

RBF with global support	$\varphi(r)$
Spline type (R_n)	$r^n, n\ odd$
Thin plate spline (TPS_n)	$r^n \log(r), n\ even$
Multiquadric (MQ)	$\sqrt{1+r^2}$
Inverse multiquadric (IMQ)	$\frac{1}{\sqrt{1+r^2}}$
Inverse quadratic (IQ)	$\frac{1}{1+r^2}$
Gaussian (GS)	e^{-r^2}
RBF with compact support	$\varphi(r) = f(\xi), \xi \leq 1, \xi = \frac{r}{R_{sup}}$
Wendland C^0 (C0)	$(1-\xi)^2$
Wendland C^2 (C2)	$(1-\xi)^4(4\xi+1)$
Wendland C^4 (C4)	$(1-\xi)^6\left(\frac{35}{3}\xi^2+6\xi+1\right)$

$\varphi(r) = r$



$\varphi(r) = r^3$



Radial Basis Functions background

- Scalar Function values g_{s_i} known at sources $\boldsymbol{x}_{s_i}$
- Orthogonality condition
- Linear polynomial

$$s(\boldsymbol{x}_{s_i}) = g_{s_i}, 1 \leq i \leq N$$

$$\sum_{i=1}^{N} \gamma_i p(\boldsymbol{x}_{s_i}) = 0$$

$$h(\boldsymbol{x}) = \beta_1 + \beta_2 x + \beta_3 y + \beta_4 z$$

$$\sum_{i=1}^{N} \gamma_i = \sum_{i=1}^{N} \gamma_i x_{k_\mathrm{i}} = \sum_{i=1}^{N} \gamma_i \mathrm{y}_{k_\mathrm{i}} = \sum_{i=1}^{N} \gamma_i z_{k_\mathrm{i}} = 0$$

Radial Basis Functions background

- Linear system to be solved for the computation of unknown coefficients
- System matrix
  - Constraint matrix $\boldsymbol{P_s}$
  - Interpolation matrix $\boldsymbol{M}$

$$\begin{pmatrix} \boldsymbol{M} & \boldsymbol{P_s} \\ \boldsymbol{P_s^T} & 0 \end{pmatrix} \begin{pmatrix} \boldsymbol{\gamma} \\ \boldsymbol{\beta} \end{pmatrix} = \begin{pmatrix} \boldsymbol{g_s} \\ 0 \end{pmatrix}$$

$$\boldsymbol{P_s} = \begin{pmatrix} 1 & x_{s_1} & y_{s_1} & z_{s_1} \\ 1 & x_{s_2} & y_{s_2} & z_{s_2} \\ \vdots & \vdots & \vdots & \vdots \\ 1 & x_{s_N} & y_{s_N} & z_{s_N} \end{pmatrix}$$

$$M_{ij} = \varphi\left(\left\|\boldsymbol{x_{s_i}} - \boldsymbol{x_{s_j}}\right\|\right), 1 \leq i \leq N, 1 \leq j \leq N$$

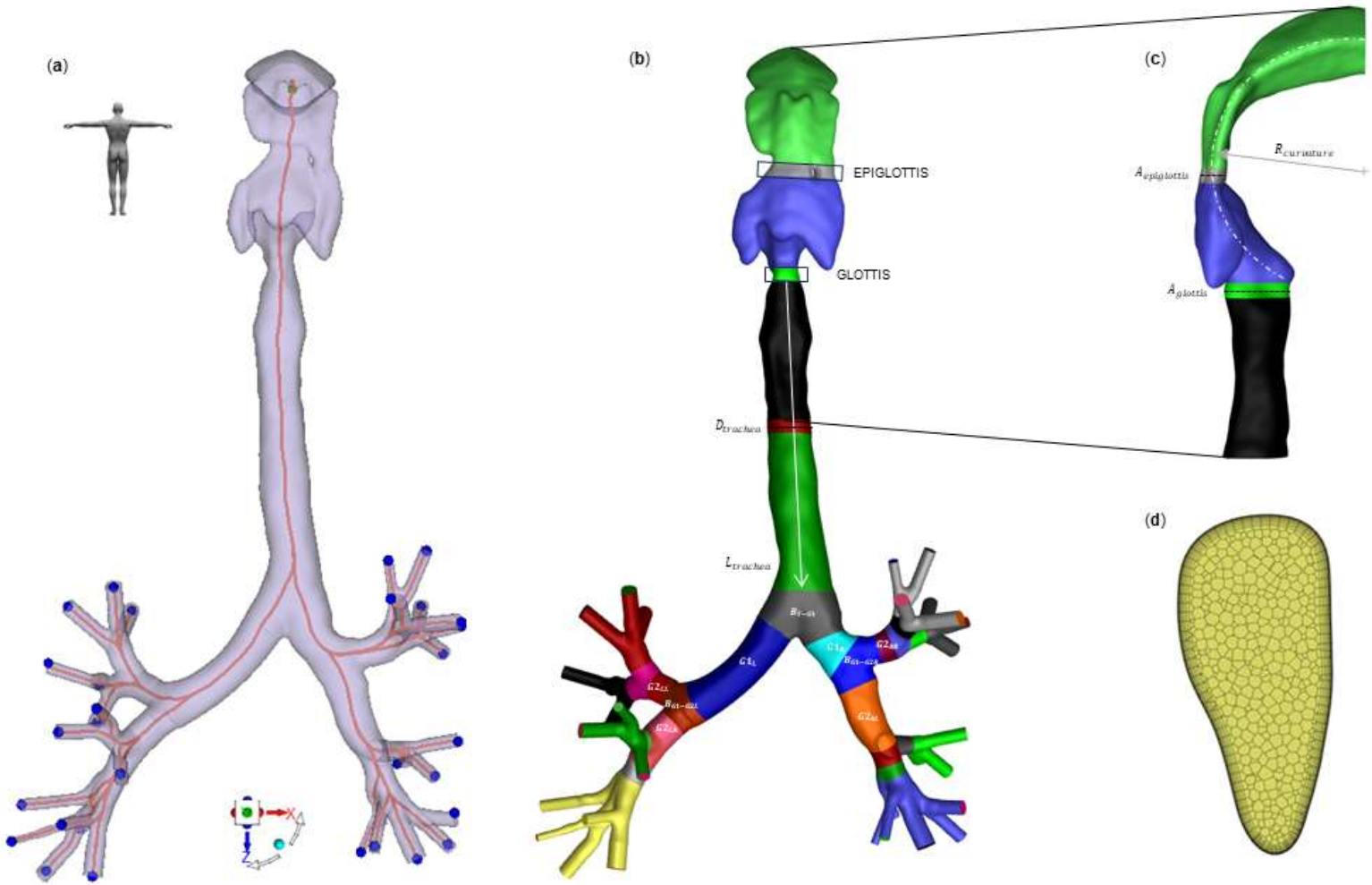
Radial Basis Functions for mesh morphing

- **Radial Basis Functions** (RBF) can be used to drive mesh morphing (smoothing) from a list of source points and their displacements.
  - Surface shape changes (exact nodes control)
  - Volume mesh smoothing.
- RBF are recognized to be one of the **best mathematical tool** for mesh morphing.

$$\begin{cases} s_x(\boldsymbol{x}) = \sum_{i=1}^{N} \gamma_i^x \varphi\left(\left\|\boldsymbol{x} - \boldsymbol{x_{s_i}}\right\|\right) + \beta_1^x + \beta_2^x x + \beta_3^x y + \beta_4^x z \\ s_y(\boldsymbol{x}) = \sum_{i=1}^{N} \gamma_i^y \varphi\left(\left\|\boldsymbol{x} - \boldsymbol{x_{s_i}}\right\|\right) + \beta_1^y + \beta_2^y x + \beta_3^y y + \beta_4^y z \\ s_z(\boldsymbol{x}) = \sum_{i=1}^{N} \gamma_i^z \varphi\left(\left\|\boldsymbol{x} - \boldsymbol{x_{s_i}}\right\|\right) + \beta_1^z + \beta_2^z x + \beta_3^z y + \beta_4^z z \end{cases}$$

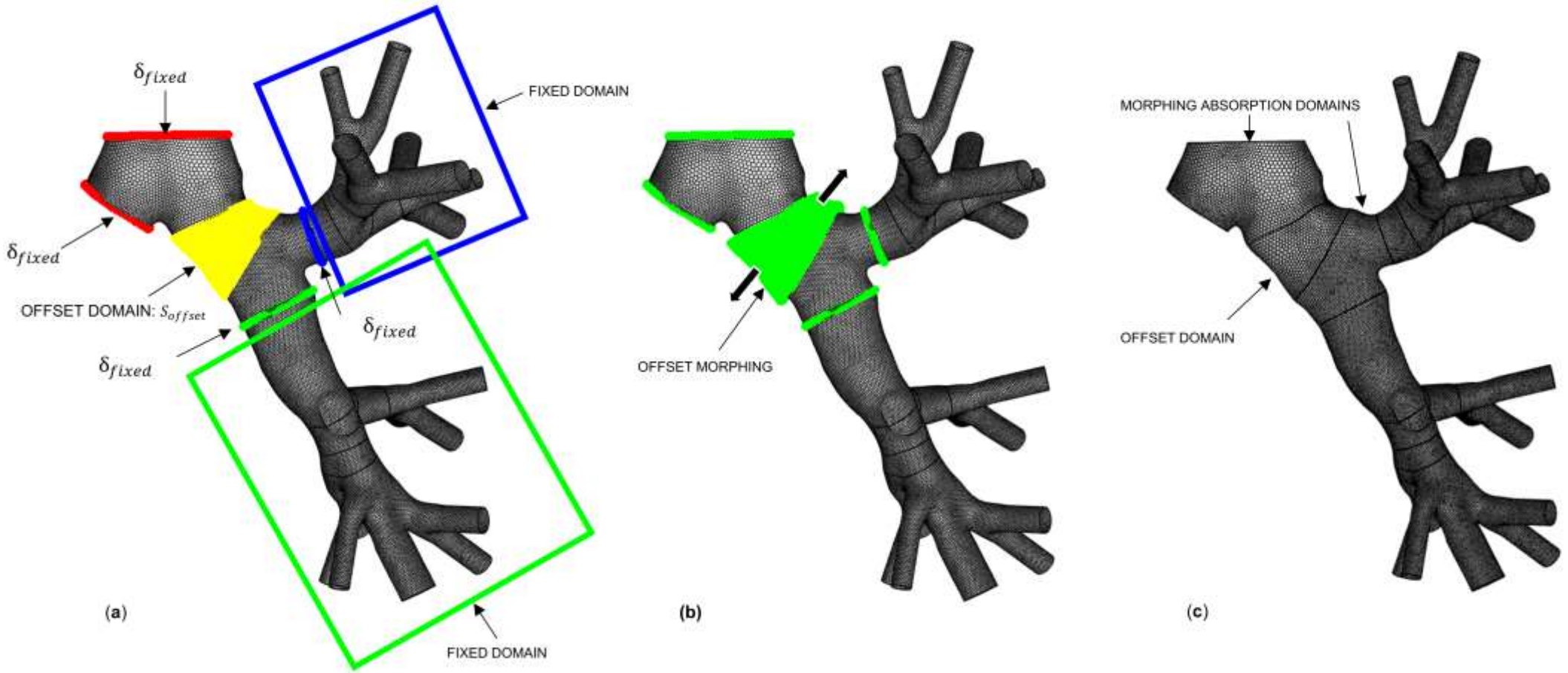
Parametric airways

- Surface segmentation
- Hierarchical tree structure
- Full automatic morphing via Python script
- Stand Alone RBF Morph API
- Final volume morphing on the baseline CFD model (could be a different mesh)



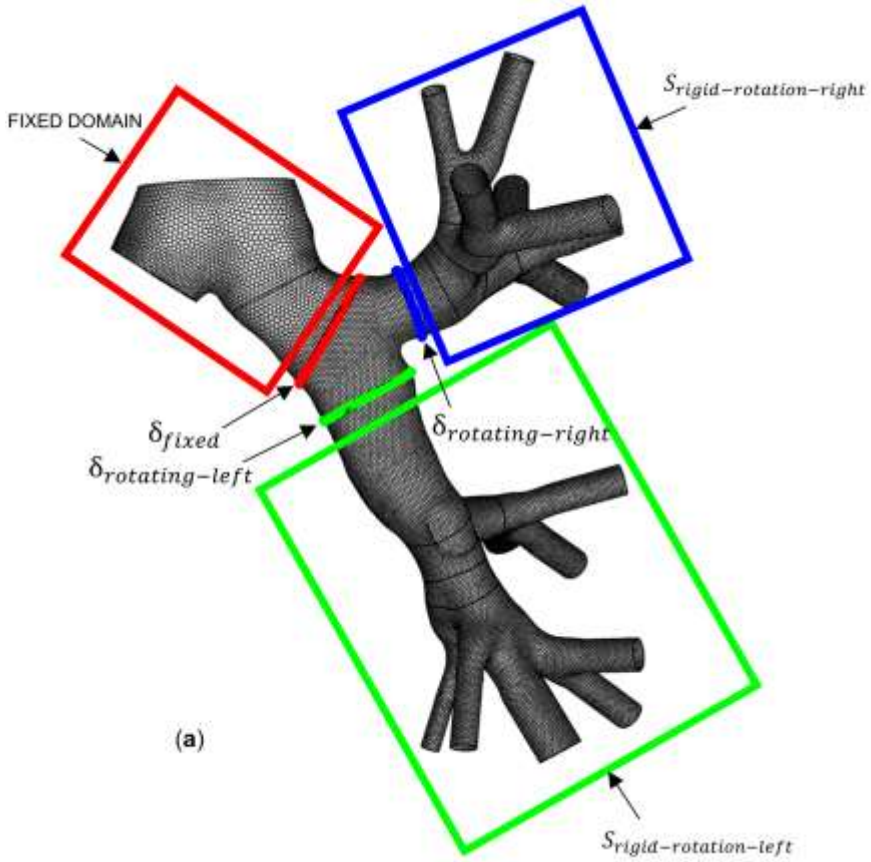
Parametric airways

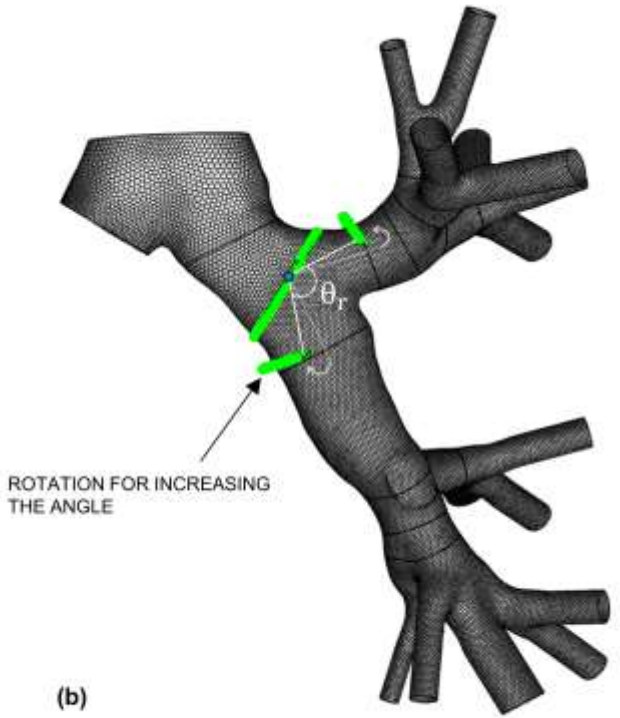
- Offset to control the diameter

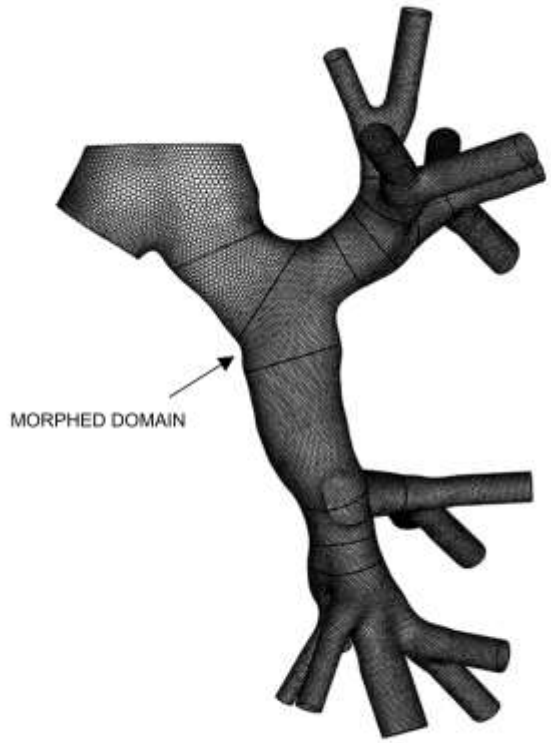


Parametric airways

- Rotation and translation to control shape and lenghts

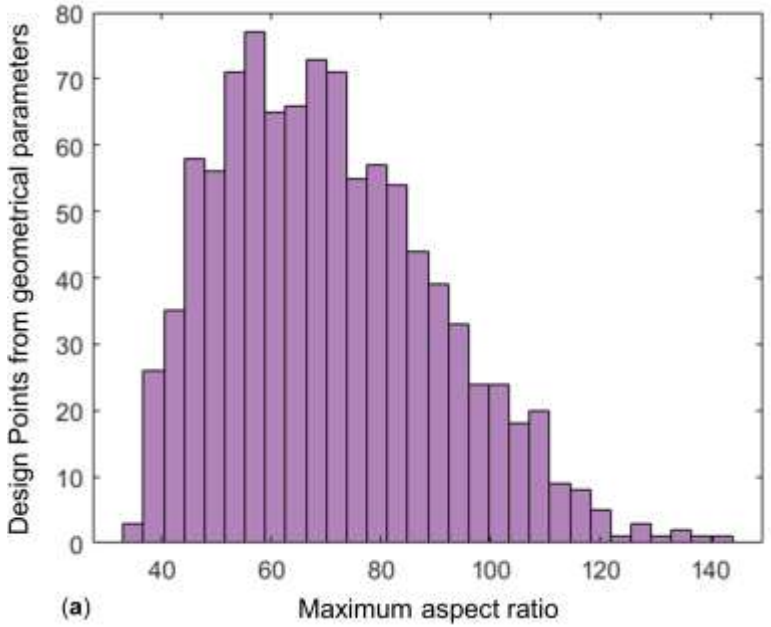


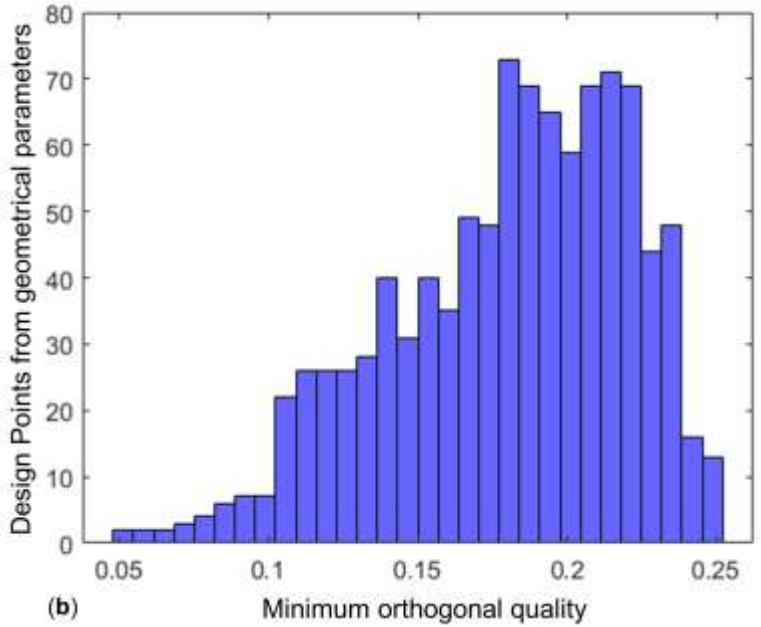




Parametric airways

- Mesh statistics for explored shapes





REAL-TIME SIMULATION

Learning

Set of pre-computed CFD simulations using ANSYS Fluent

SHAPE MODE 1 — PHYSICAL MODE 1

SHAPE MODE 2 — PHYSICAL MODE 2

⋮ — ⋮

SHAPE MODE r — PHYSICAL MODE k

$r \neq k$

High-fidelity simulation results: **LEARNING SNAPSHOTS**

ROM GENERATION

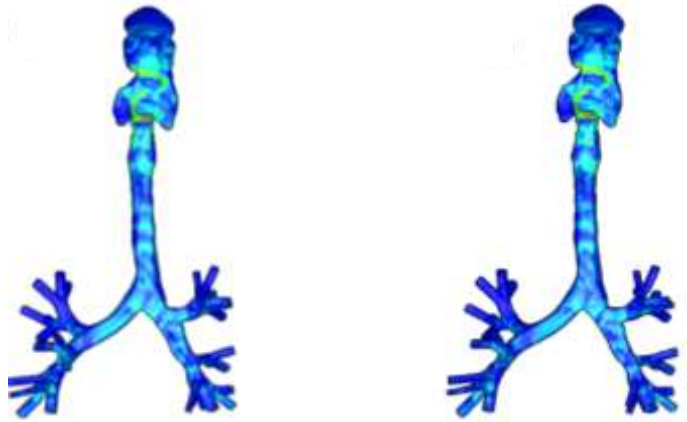
Repeated for all the output variables

Validation

OFFLINE PHASE

Using the left-out configurations

HIGH-FIDELITY SIMULATION — **ROM SCENARIO**



Error assessment between ROM and high-fidelity solution

Consumption

ONLINE PHASE

ROM CONSUMPTION

Real-time evaluation of the simulation results

Deployment

ROM EXPORTATION

Connection and input/output ports generation for the TWIN

TWIN GENERATION

FMU DEPLOYMENT

REDUCED ORDER MODELING

- Using Static ROM Builder in Ansys Twin Builder

- Considering 26 shape parameters. ☑
- Based on grid transformations using radial basis function (RBF) mesh morphing. ☑
- Executed on both surface and volume meshes. ☑
- Correctly validated. ☑

- Combining 26 shape parameters + 3 physical parameters. ☑
- Implemented for parameters of clinical interest:
  - Accretion rate
  - Pressure
  - Turbulent kinetic energy ☑
  - Velocity
  - Wall shear stress
- *Partially* validated. ☑

MODEL ORDER REDUCTION

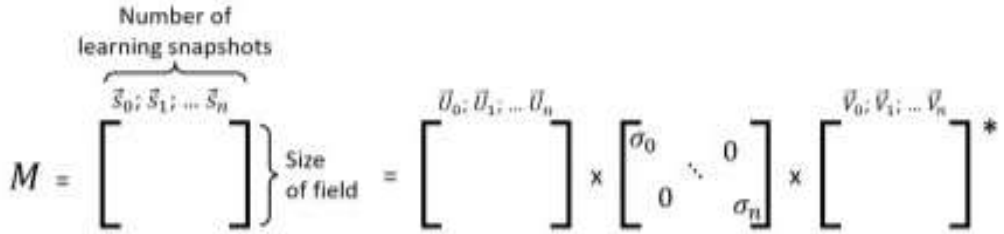
... SNAPSHOT GENERATION ... → SNAPSHOT MATRIX (M)

↓

SINGULAR VALUE DECOMPOSITION

PROPER ORTHOGONAL DECOMPOSITION (POD)

$$M = U\Sigma V$$



U and V are orthogonal matrices and Σ is a diagonal matrix containing the singular value

↓

MODES SELECTION

Based on the magnitude of the corresponding singular values. These modes capture the most significant properties of the system.

↓

REDUCED ORDER BASIS

Constructed by selecting a subset of columns from the matrix U.

↓

PROJECTION

The full-order system is projected onto the reduced order basis to obtain a lower-dimensional system

ROM ERRORS

(1) The Reduction Relative error represents the mean error projection of the vectors used to calculate the *r* modes (SVD).

$$\textit{Reduction Relative error} = \frac{\|M - M_r\|}{\|M\|} = \frac{\sum_{i=r+1}^{n} \sigma_i^2}{\sum_{i=1}^{n} \sigma_i^2} \qquad (1)$$

The number of shape modes used should be selected according to (1)

In other words, it is the error that is made in using a small number r of modal components.

(2) The other error is the ROM relative error which is the difference between the high-fidelity snapshot X_{ref} and the ROM-built snapshot X_{ROM}.

$$\text{ROM relative error} = \frac{\|X_{ref} - X_{ROM}\|}{\|X_{ref}\|} \qquad (2)$$

ROM validation should be performed on the excluded snapshots using (2)

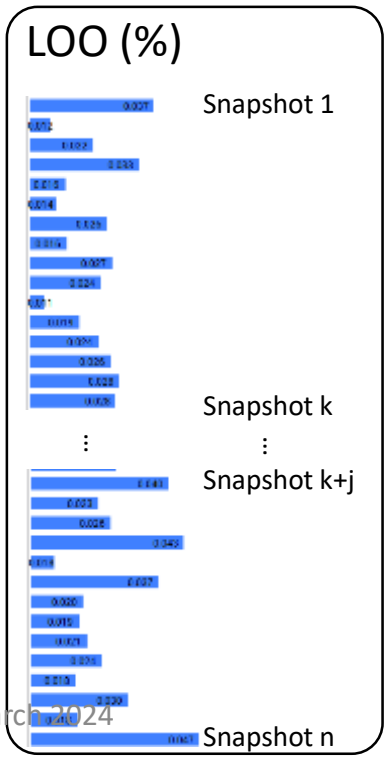
The ROM relative error therefore also takes projection errors into account.

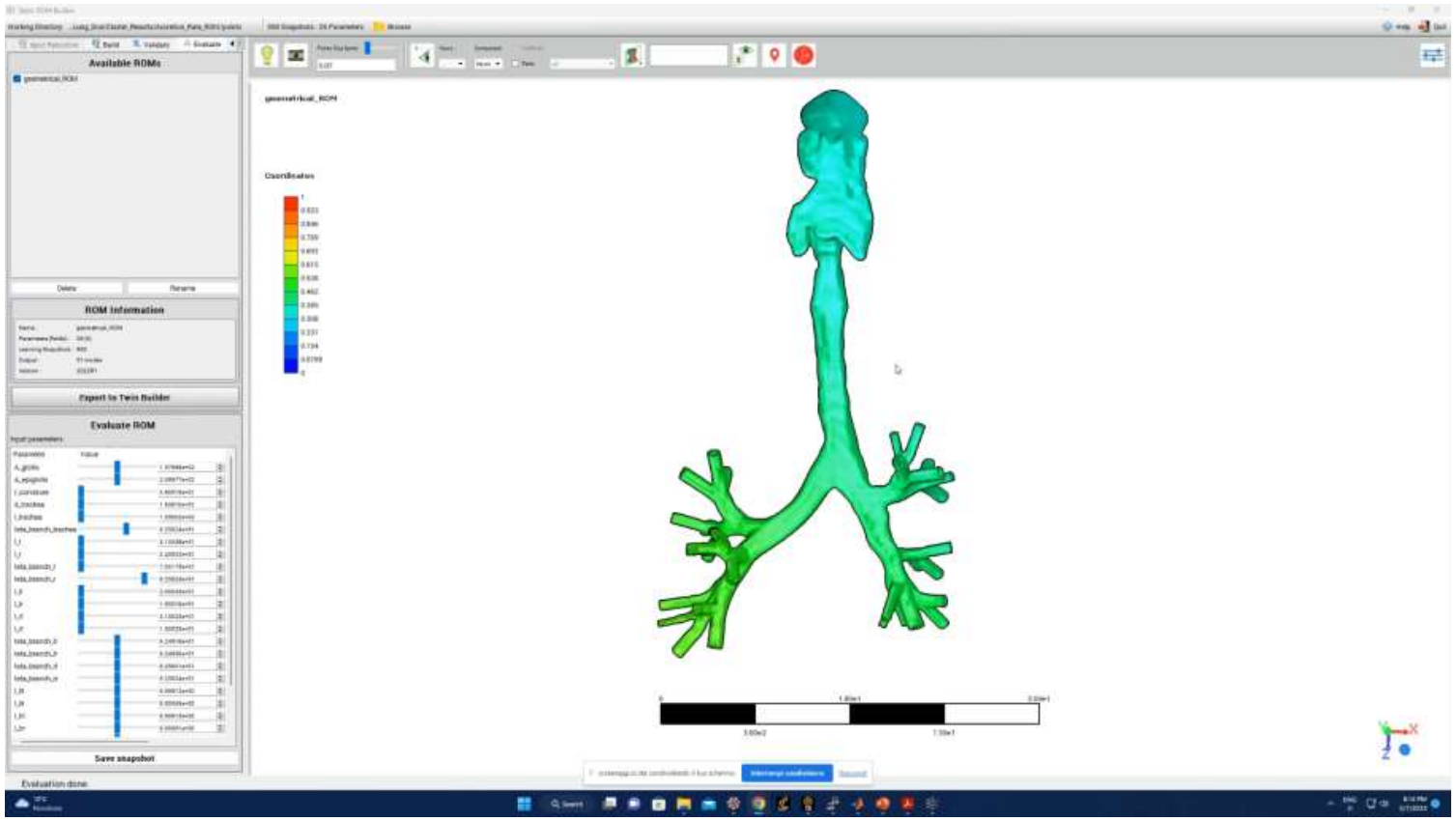
GEOMETRIC REDUCED ORDER MODEL(s)

If 200 snapshots are used: 1 hour of calculation for the building.

960 snapshots are used: 12 hours of calculation for the building.

The leave-one-out (LOO) cross-validation demonstrates that ROM is able to correctly represent new unseen shapes.

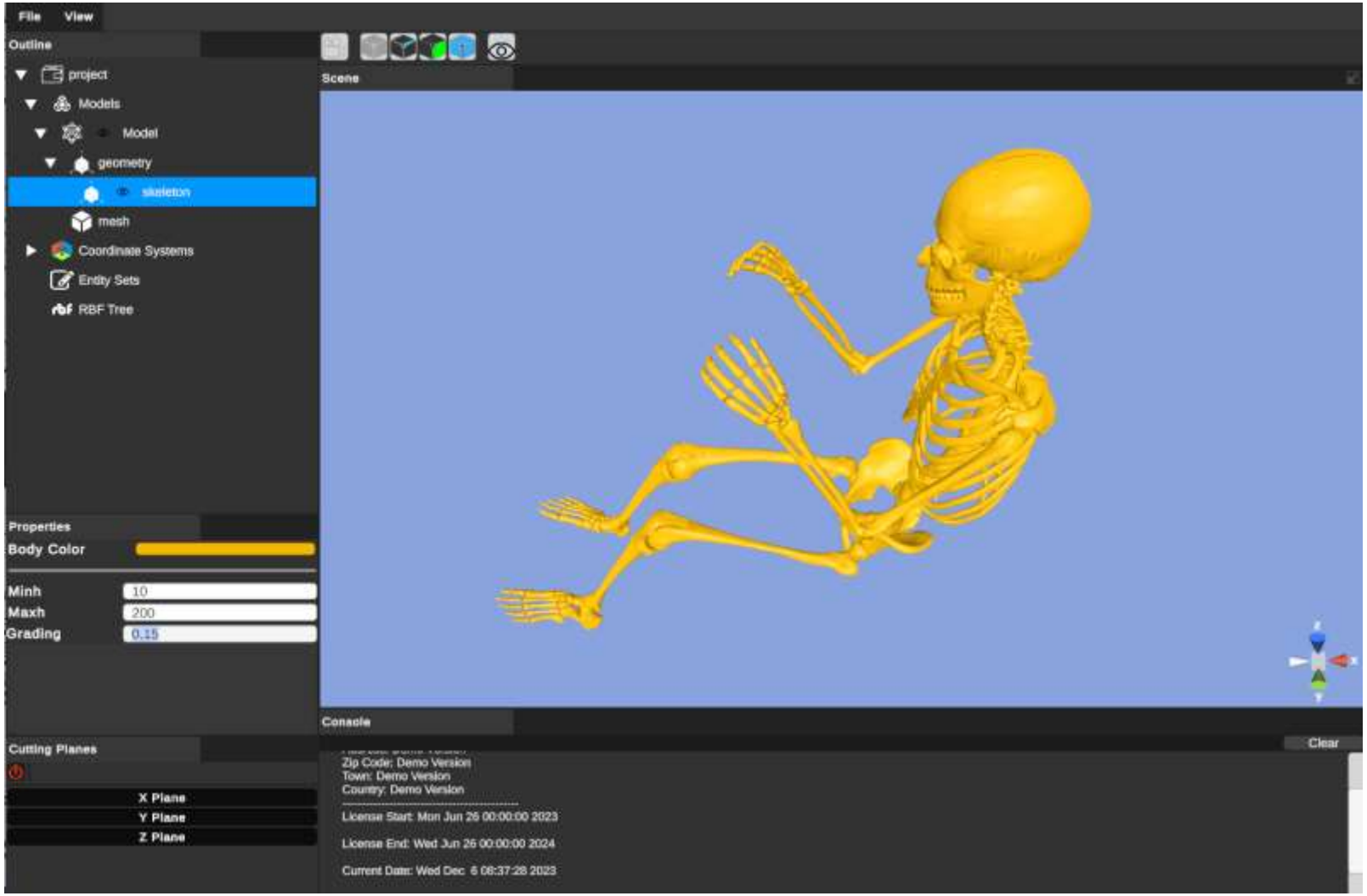




Conclusions

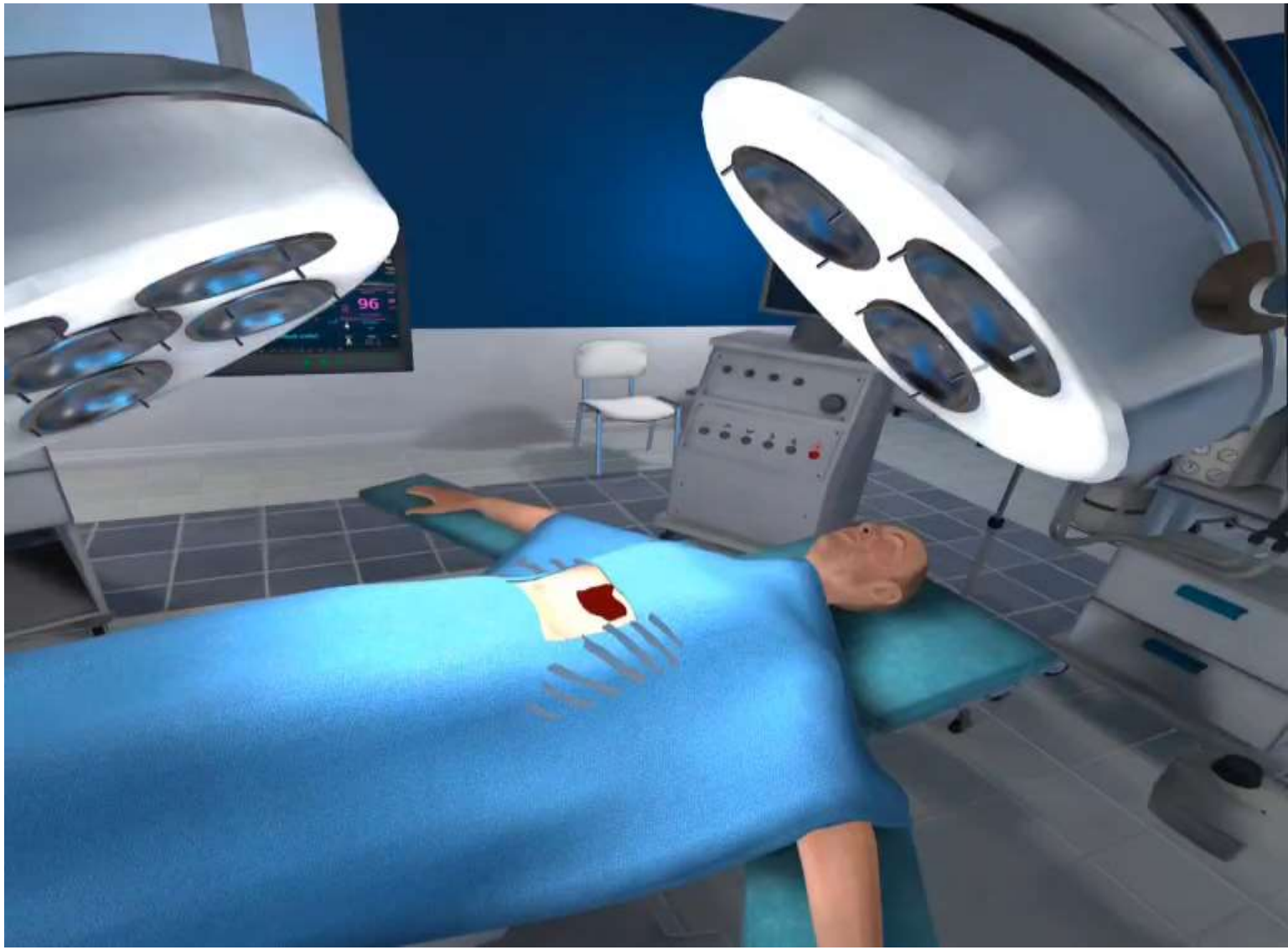
- Medical Digital Twins are feasible today!
- The **In Silico** path, i.e. MDT driven by high fidelity simulations, is ready and requires
  - Patient specific data (from images)
  - State of the art multi-physics simulation
  - Reduced order models and advanced mesh morphing
- A clear **business model** is required
  - Public funds are today the major resource
  - Certification is complex
- We are moving in the right direction and there is **mainstream focus** on Medical Digital Twins

Next steps? New RBF Morph Stand Alone



- To be released in 2024
- Read in **STL, STEP**
- **Unity - OpenCascade**
- Solver independent process that supports **many mesh formats**
- **Scriptable** via python

Next steps? AR/VR



Thank you!

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