InSilicoTrials

Synthetic patients in a workflow for orthopedic device testing

OSMA 2025 Spring Event
Annapolis, Maryland
April 22-24, 2025

Computer simulations are standard technology for many industries

100% of new cars and airplanes are developed and tested

Using modeling and simulation

Automotive

Aerospace

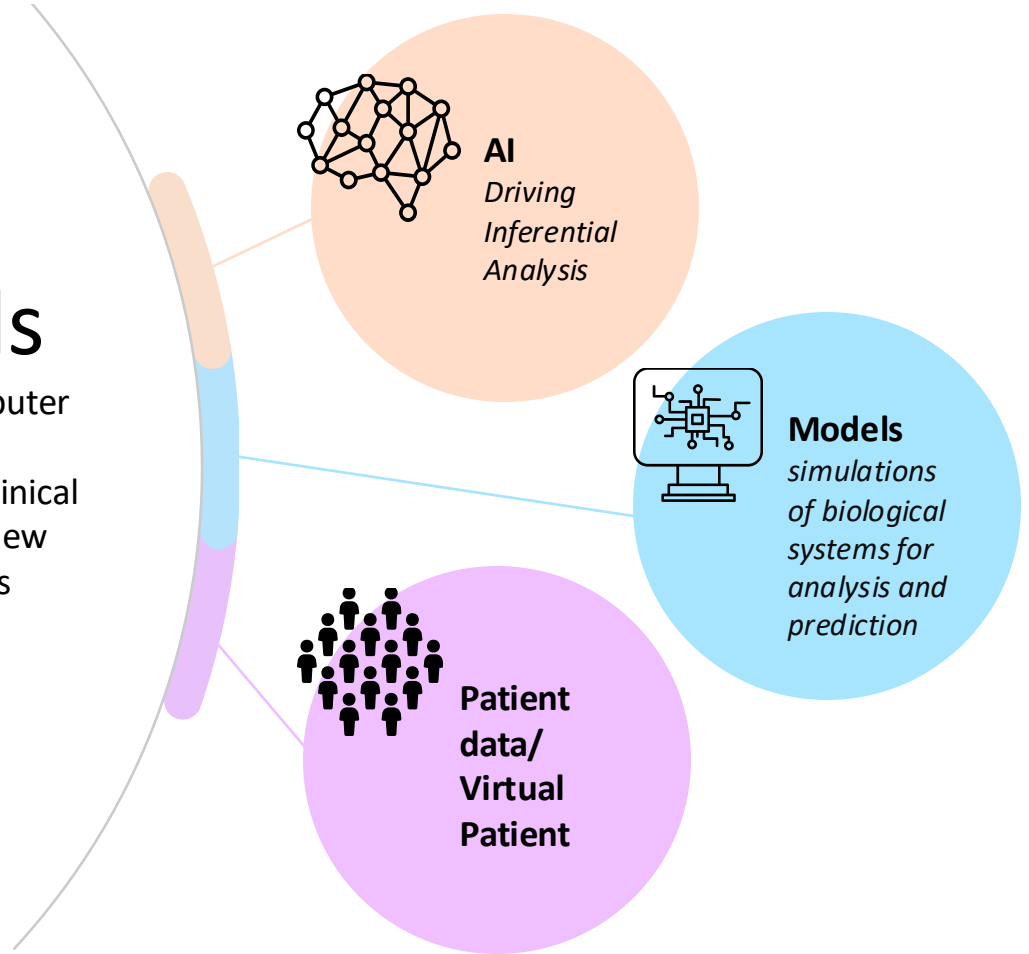
But modeling and simulation is underutilized in the healthcare industry

What is an *in silico* trial?

Mainstream definition by scientists and regulators

in silico trials

the use of individualized computer simulations in the design, development or nonclinical, clinical and regulatory evaluation of new drugs, devices or interventions



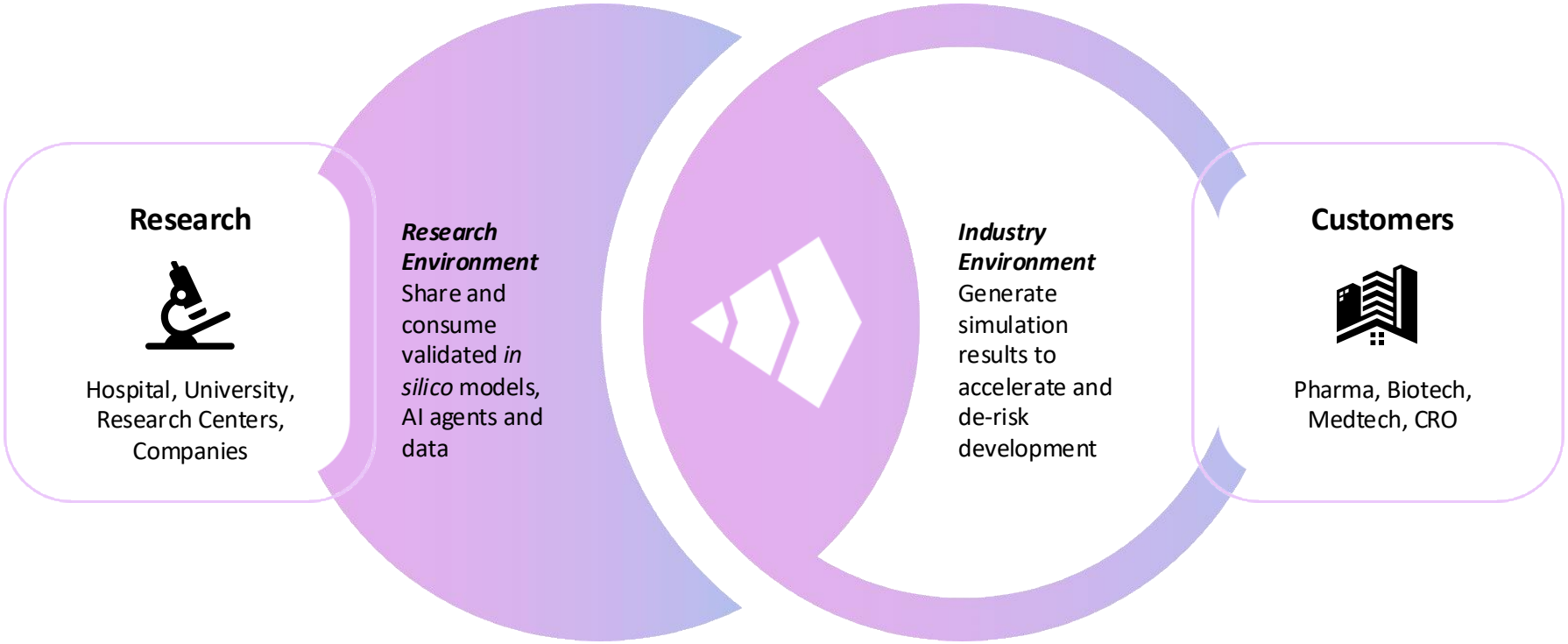
Main advantages of conducting *in silico* trials:

- Cost Reduction
- Time Efficiency
- Reduced Ethical Concerns
- Exploration of Complex Systems
- Prediction and Optimization

InSilicoTrials Leading Scientific Platform for In Silico Evidence Generation

A Collaborative Ecosystem of 70+ renowned Universities and Research Centers and 50+ Data Providers

Fully aligned with regulatory guidance by US FDA and EMA



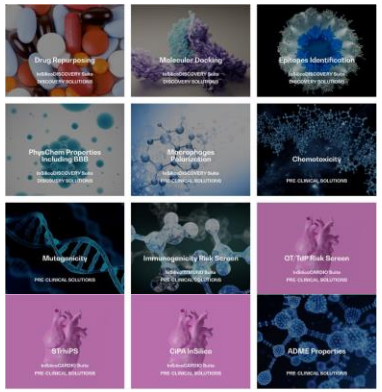
U.S. FOOD & DRUG ADMINISTRATION

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

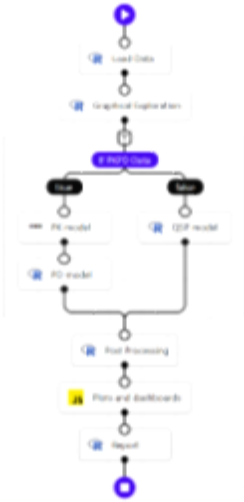
InSilicoTrials' Platform

Accelerate clinical trials while reducing risk

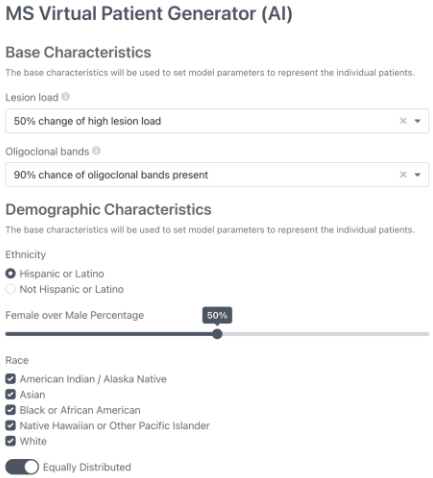
Integrate Validated models and data



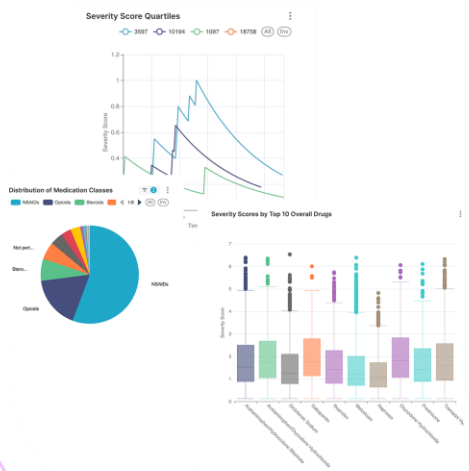
Orchestrate Models to simulate clinical trials



Virtual Patients Generator

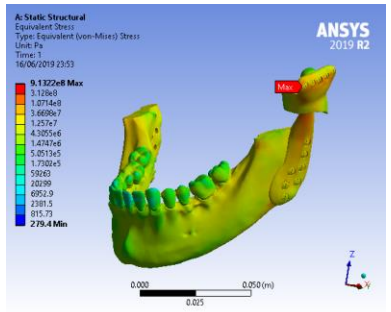


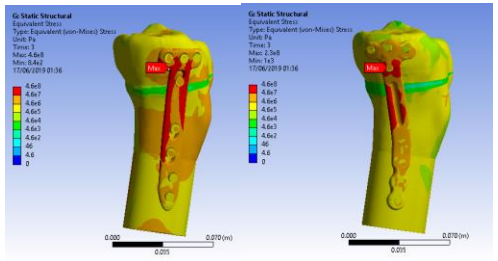
Generate Multi-level Digital Evidence

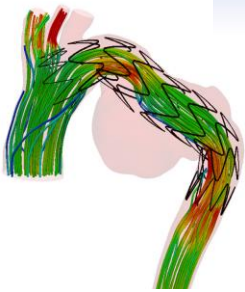


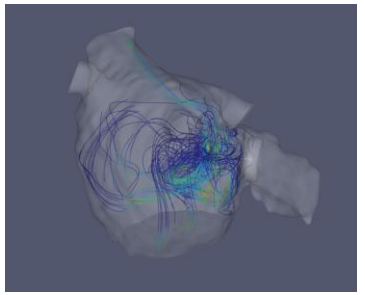
In Silico Testing of device-body interaction

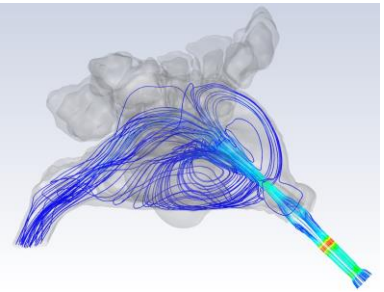
- **Predictions** on **implant effects** and **interaction** with human tissues/anatomy
- Identifying potential risks and enhancing patient safety
- Compare the product with competitors on the market
- Biocompatibility assessments focusing on understanding the interaction between devices and biological systems
- Analysis of combinational products to facilitate the optimization of drug delivery mechanisms and dosage strategies

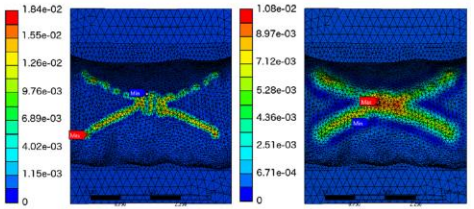










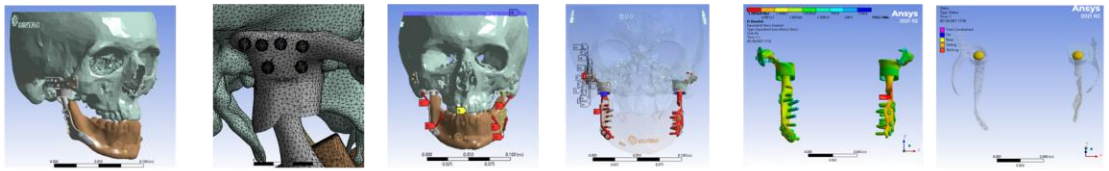


(a) 1 day, plaque (b) 7 days, plaque

Virtual Patients for Medical Devices

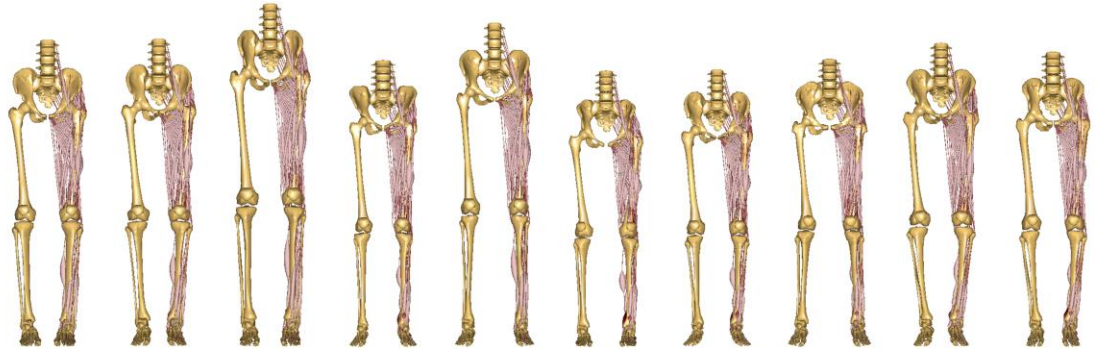
Patient-specific simulations

- Predict deployment effects and simulate different treatment options, such as device sizing, positioning, anatomical alignment, etc.
- Provide critically important insights and valuable support to the medical decision, whether related to diagnosis, prognosis or treatment planning
- Personal, predictive and preventive medicine.



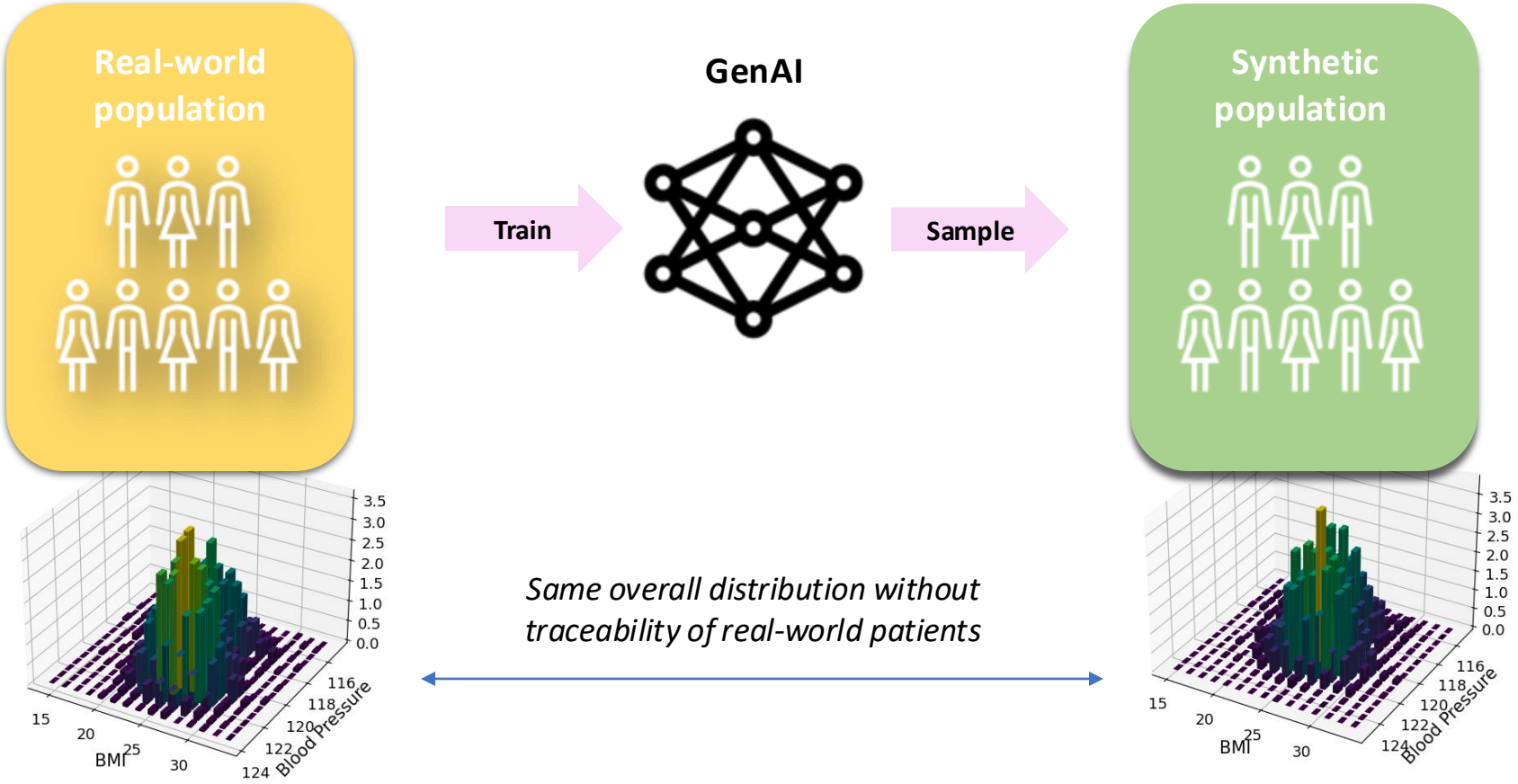
In Silico Trials on Virtual Population

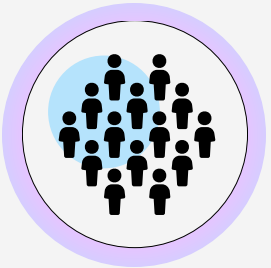
- Test safety and efficacy of new medical device by performing multiple “virtual surgical procedures”.
- Identify worst-case scenarios, highlight features needing revision, predict the device success rate.
- Reduce, refine, and replace in vivo clinical trials in terms of cohort size and time duration.
- Add digital evidence for under-represented or underserved populations (e.g., pediatric, rare disease)



Synthetic Patients

Capturing as many of the complexities of the original anatomical and (patho)physiological dataset, but that does not actually include any real patient data





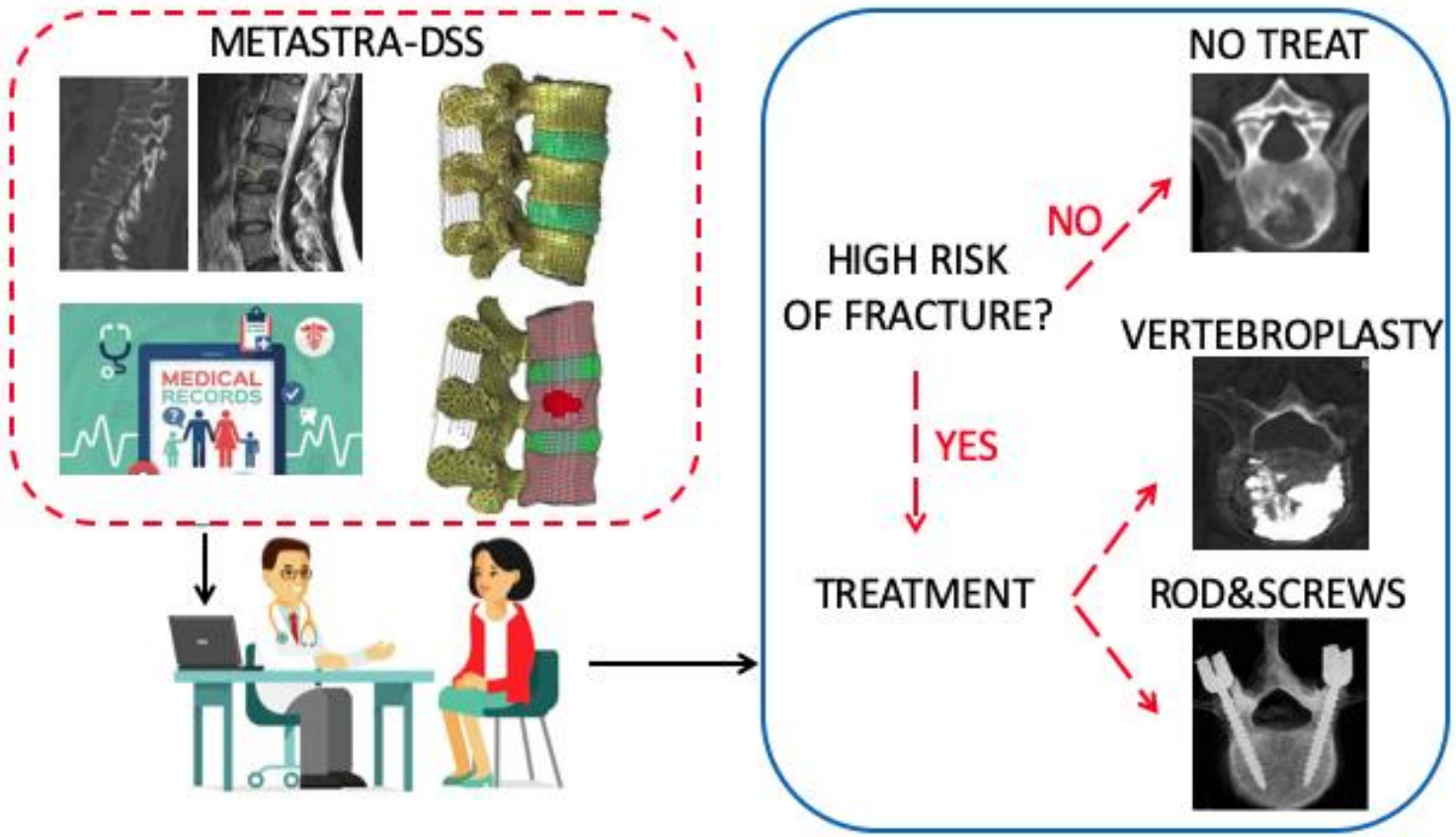
- Patient centered care, safe and ethical trials
- Enhanced study data privacy and security
- De-risking programs
- Augment minority groups for what-if scenarios

Patient-specific simulations:

METASTRA

GOAL OF THE PROJECT

- Develop a **Decision Support System (DSS) to revolutionise treatment** for patients with vertebrae metastases
- AI and Biomechanics computational models
- Accurate **risk stratification** & **personalised** surgical recommendations
- Reduce uncertain diagnoses from **60% to 20%**



Funded by the European Union

Patient-specific simulations:

Detailed modeling strategy to be adopted for the most difficult cases

Multiscale models:

- Subject specific anatomy
- Detailed lesion modeling
- Subject-specific material properties

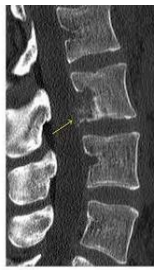
Finite element sub-models:

- Healthy bone tissue
- Metastatic tissue
- Intervertebral discs
- Interfaces

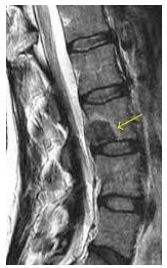
Required intervention:

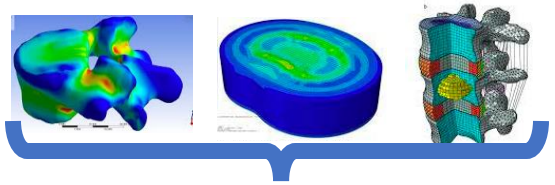
- Experienced operator
- Semi-automated tools

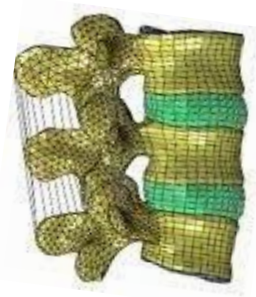
CT



MRI

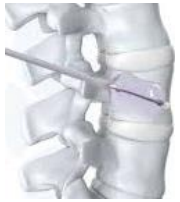




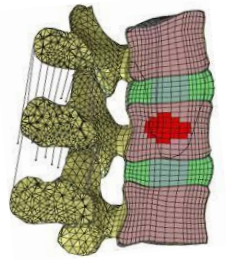


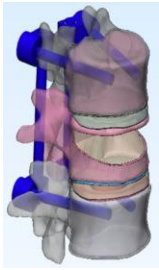
Risk of fracture

Cement



Implant





Optimal surgical parameters

Funded by the European Union

In Silico Trials: Virtual High Tibial Osteotomy Surgery

Assessment of mechanical safety equivalency between 3D-printed personalized and generic high tibial osteotomy devices

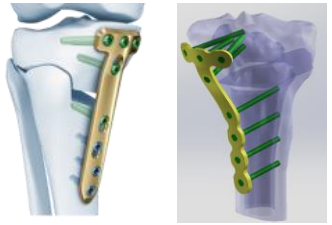
INPUT

PATIENT-SPECIFIC MODELING

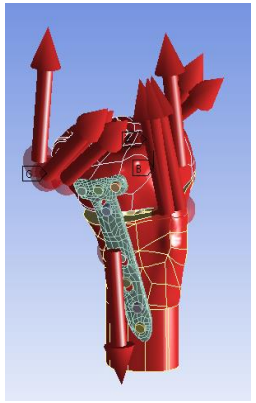
OUTPUT

30 Knee Arthritis Patients

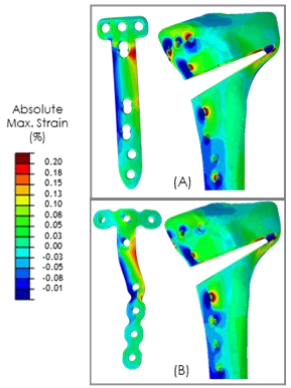
CT segmentation and bone material properties extraction

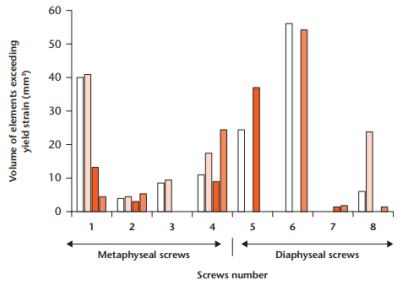


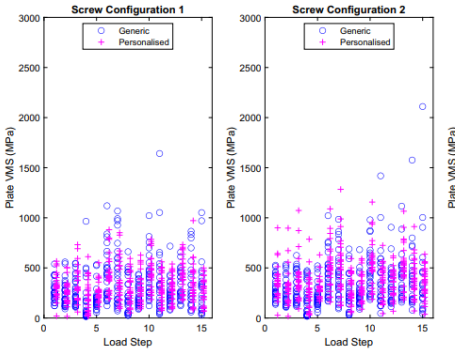
Virtual HTO Surgery



Muscle and joint forces during Activities of Daily Living







Results comparison

[TOKA: The Tailored Osteotomy for Knee Alignment System]

MacLeod et al., https://doi.org/10.1302/2046-3758.712.BJR-2018-0035.R1; MacLeod et al., https://doi.org/10.1038/s43856-021-00001-7

Our engagement in Regulatory Science

We wrote the book *Toward Good Simulation Practice*

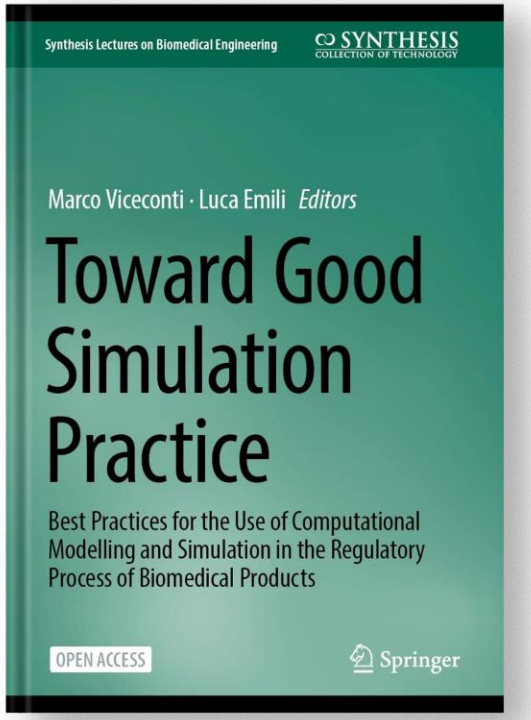
13
FDA members

U.S. FOOD & DRUG ADMINISTRATION

&

130+
researchers from university and industry

Johnson & Johnson
Boston Scientific
Medtronic



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*Nature Publishing Group: Over 40,000 copies distributed as of April 2025.

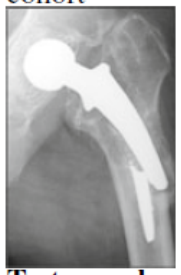
Toward Good Simulation Practice – The Book

Table of contents

Toward Good Simulation Practice: Model Credibility

Example of model validation using population-based data from a clinical study

Table 4.4 Example of validation of an FEA model predicting the fatigue strength of a hip stem during daily living activities

Question of interest	Context of use (CoU)	Computational model	Clinical comparator	Assessment
Does the proposed hip stem design have sufficient strength to prevent implant fracture in patients?	FEA is used to assess the occurrence of fracture of the hip stem in a virtual patient cohort to enrich clinical data for those configurations which have low (or no) real patient numbers	An FEA model of a hip stem with system conditions reproducing the expected biomechanical environment and loading conditions during activities of daily living  **Sensitivity** of the results to the loading conditions and CT-based bone material properties **Uncertainty** in the cortical bone thickness based on the CT segmentation is propagated through the model	Stem fracture location and rate in a clinical study of a similar hip stem in a patient cohort  **Test samples:** Statistically significant number of patients were enrolled following standard practises, covering a wide range of demographics **Test conditions**: The implant was subjected to a wide range of daily activities, based on clinical scores	Computational model vs Comparator **Input comparison**: The types of all inputs are similar, but the ranges are not necessarily equivalent (demographics, load) **Output comparison:** Fracture location (visual) and rate were captured in the clinical study and predicted by the FEA models Fracture rate and location in the virtual cohort were compared to the fracture rate and location in the clinical comparator

Courcelles, E. *et al.* (2024). Model Credibility. In: Viceconti, M., Emili, L. (eds) Toward Good Simulation Practice. https://doi.org/10.1007/978-3-031-48284-7_4

Toward Good Simulation Practice… and beyond

The aspiration is that this book will:

- Spark more dialogue among all parties involved.
- Set the stage for future development of standards that could significantly impact the safety, efficacy, and regulatory compliance of medical products.
- Lead to the creation of widely recognized and community-adopted Good Simulation Practice, advancing the use of modeling and simulation in medical product development.

Thank you

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