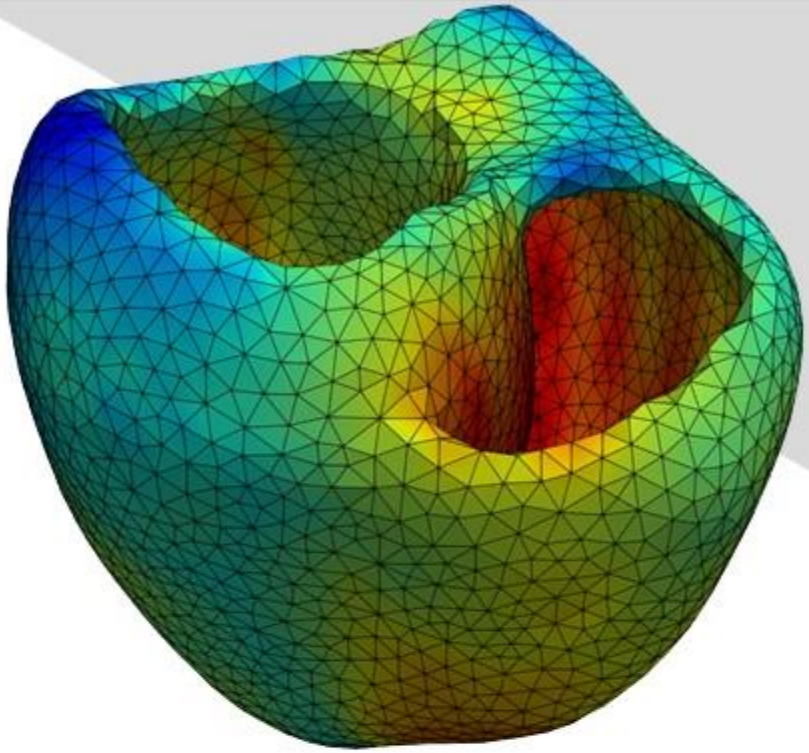

From technological readiness to evidence requirements: What is still needed to implement in-silico clinical trials in regulatory practice?

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From technological readiness to evidence requirements

In-silico clinical trials – a look back

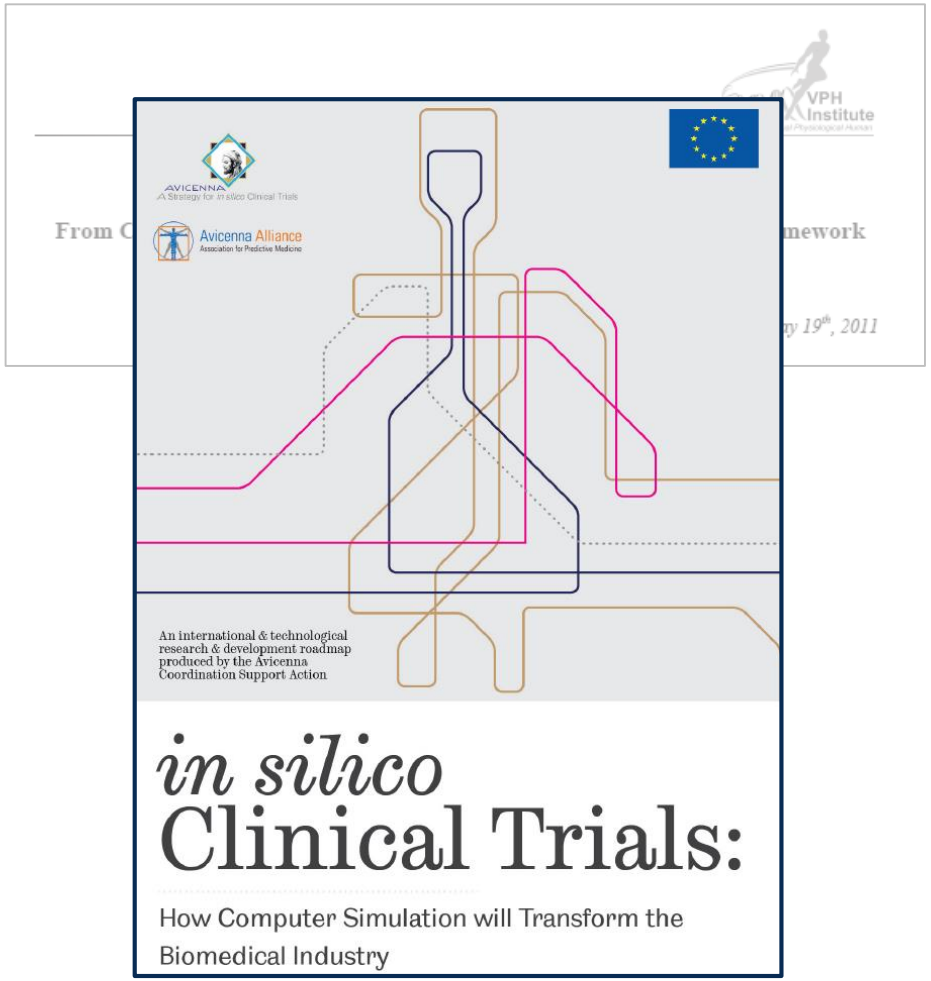
2011

"We **recommend** a parallel program that in the next framework should be limited to targeted research, **entitled in silico clinical trials**, which targets the use of ICT to simulate how large cohorts would react to new drugs, medical devices, biotech and tissue engineered products.

If proved effective these new technologies could be positioned before real animal and clinical trials, in order to increase the efficacy of their design, reduce the size of the cohorts, the risks for the patients (or the invasiveness for the animals), and the costs for the biomedical industry (which could turn into a reduction of costs for these products).

It could also open an entirely new market, for In Silico Clinical Research Organisations, a new type of CRO that would conduct these simulated clinical trials on the next-generation computing cloud."

In-silico clinical trials – a look back



2015

The use of individualised computer simulation in the development or regulatory evaluation of a medicinal product, medical device, or medical intervention.

(…) developing in silico technologies to **reduce, refine and partially replace in vivo experimentation** requires overcoming knowledge, reliability, and adoption barriers.

The Avicenna roadmap extensively analyses :

- The physiological envelope
- From validation to confidence
- The physiological envelope
- Automation

Adapted from Viceconti et al., 2016

In-silico clinical trials – a look back

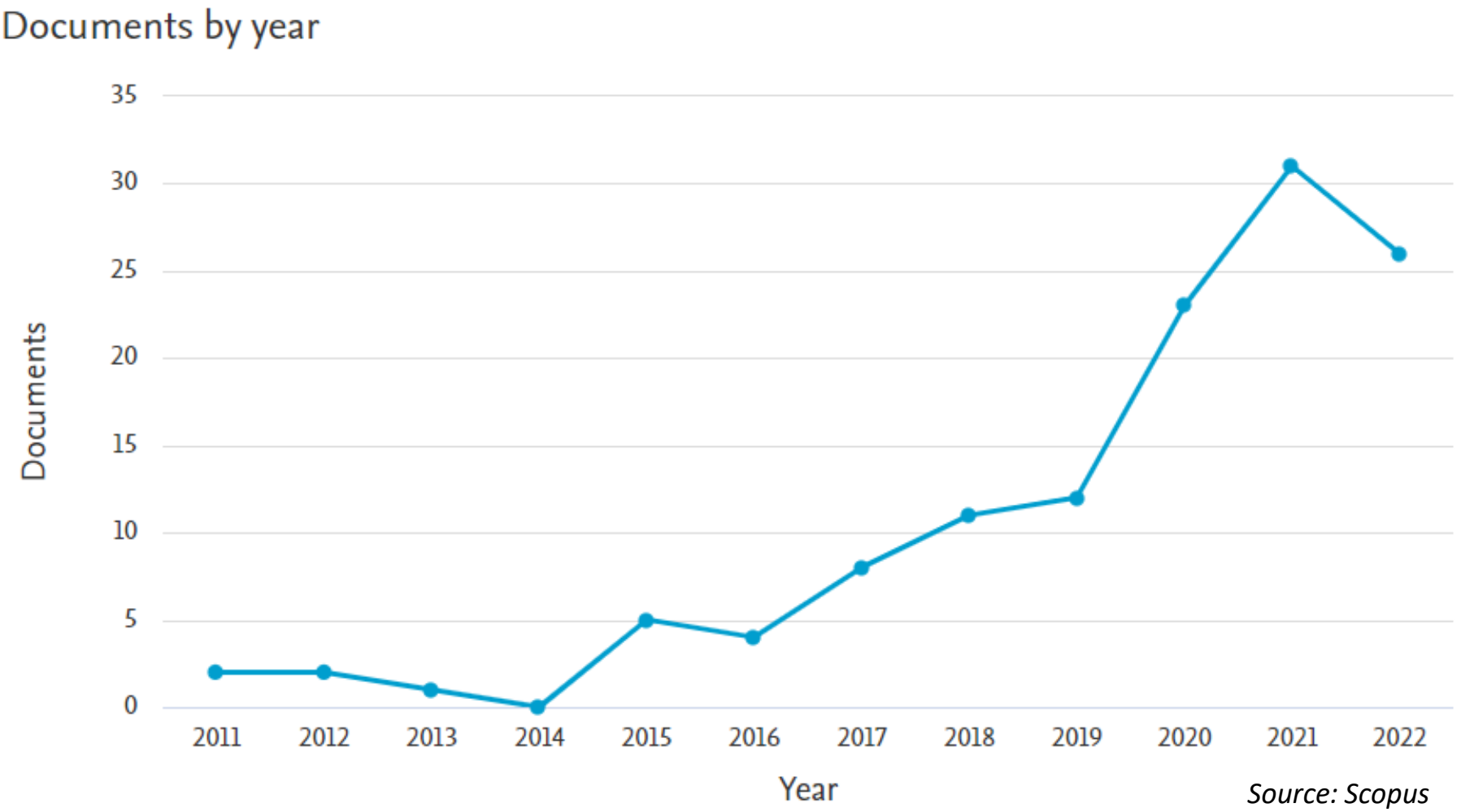
2019

"Different modelling and simulation methodologies can be used in ISCT. They range from pure computer science techniques [i.e. agent-based modelling (ABM), machine learning (ML)] to mathematical approaches (i.e. differential equations, finite elements and regression analyses).

Full-scale adoption of patient-specific modelling and simulation in healthcare and in the regulatory process is still far from reality.

Should best practice be adopted, it is possible to envisage a scenario in which a new medical product can be entirely developed and tested for safety and efficacy in silico before the product is ever manufactured."

In-silico clinical trials – Examples of early adoption



Source: Scopus
Keywords: in silico clinical trials

In-silico clinical trials – Examples of early adoption

Drug Development

Device Testing

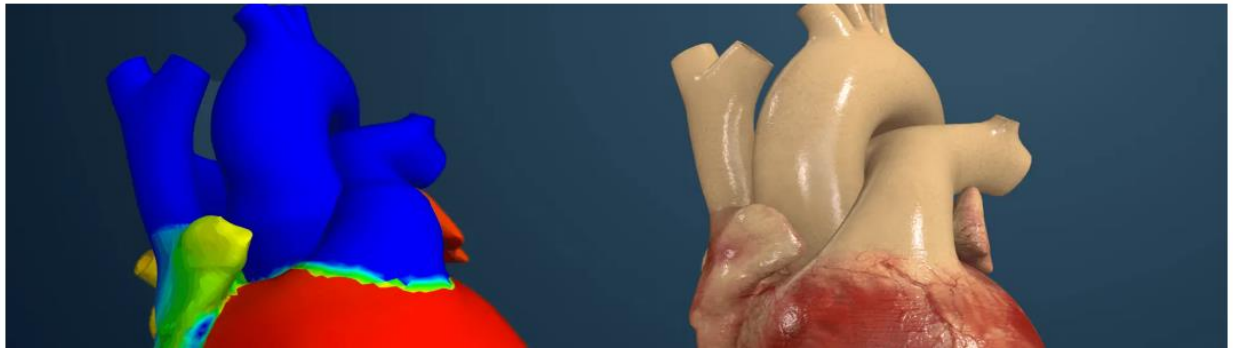
Data generation

In-silico clinical trials – Examples of early adoption

Engagement with regulatory bodies

Dassault Systèmes and the FDA Extend Collaboration to Inform Cardiovascular Device Review Process and Accelerate Access to New Treatments

- An in silico clinical trial is underway with the 3DEXPERIENCE platform to evaluate the Living Heart simulated 3D heart for transforming how new devices can be tested
- Five-year extension of their collaborative research agreement aims to spur medical device innovation by enabling innovative, new product designs
- Both Dassault Systèmes and the FDA recognize the transformative impact of modeling and simulation on public health and patient safety



What is still needed to implement in-silico clinical trials in regulatory practice?

In-silico clinical trials – The challenges

Technological Readiness	Standardization
Validation and Verification	Evidence Requirements & Regulatory guidance

In-silico clinical trials – The challenges

Technological Readiness

- Technology used needs to be sufficiently advanced and reliable
- Which TRL is considered to be ‘sufficiently advanced’
- Are different levels of TRL acceptable for different pathologies/problems

Standardization

Validation and Verification

Evidence Requirements & Regulatory guidance

In-silico clinical trials – The challenges

Technological Readiness

Standardization

- Of methods, the design of ISCT, the validation of models, and the reporting of results.
- Ensure consistency and comparability across studies
- Facilitate the regulatory evaluation of the data generated.

Validation and Verification

Evidence Requirements & Regulatory guidance

In-silico clinical trials – The challenges

Technological Readiness

Standardization

Validation and Verification

- Processes for iSCT models to ensure that they accurately represent the real-world conditions they are designed to simulate.
- Use of appropriate data sources, model calibration, and sensitivity analysis.

Evidence Requirements & Regulatory guidance

In-silico clinical trials – The challenges

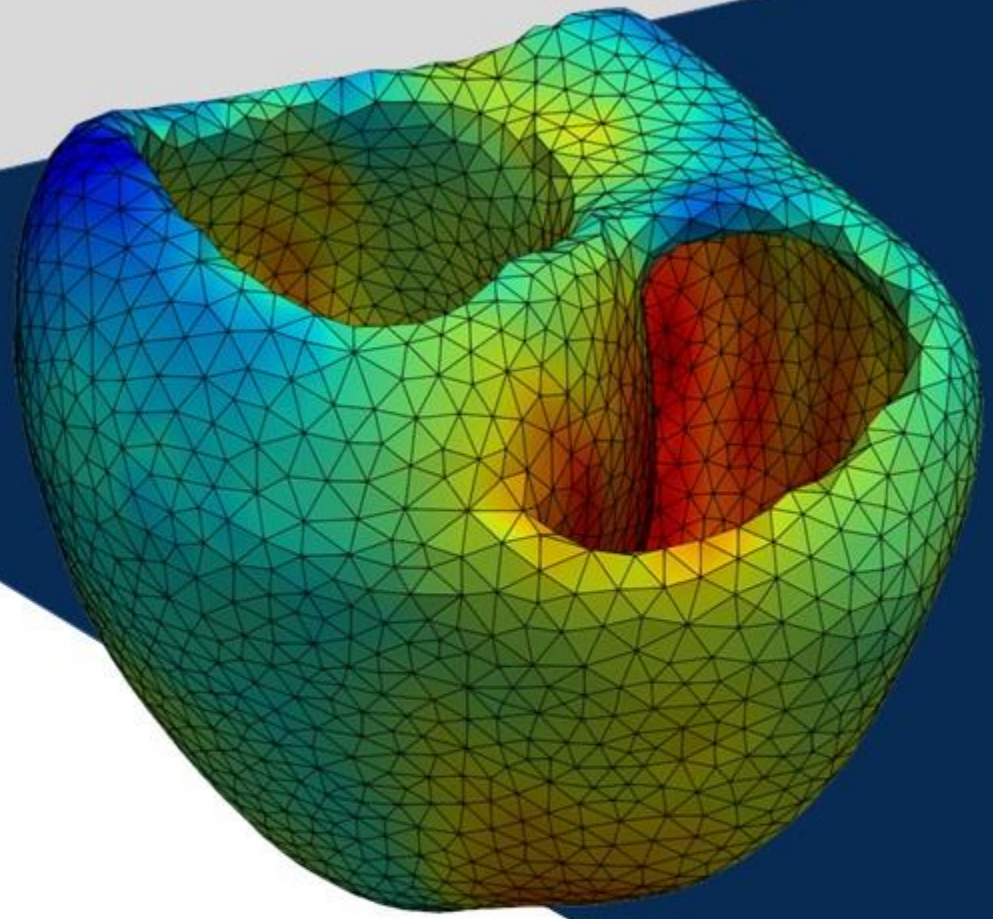
Technological Readiness

Standardization

Validation and Verification

Evidence Requirements & Regulatory guidance

- Clear guidance on regulatory decision-making
- What are acceptance criteria for iSCT evidence
- What are potential limitations and uncertainties
  What is necessary for iSCT to be used as a substitute for traditional clinical trials.



Thank you for
your participation