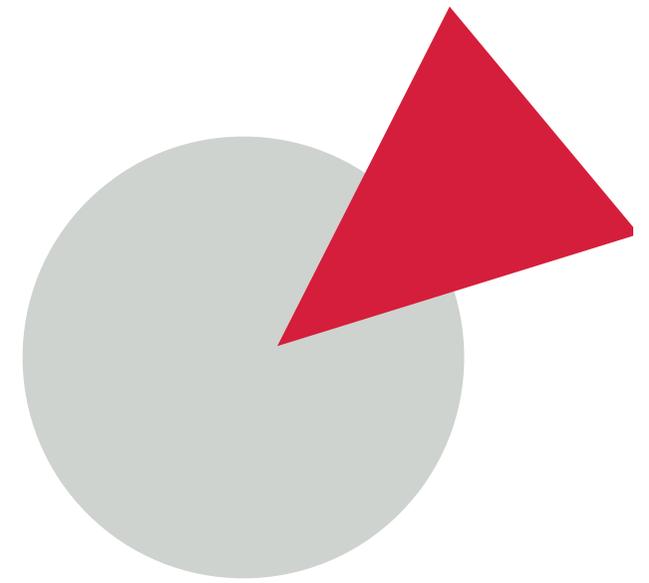


INSIGNEO

Institute for *in silico* Medicine



In silico Clinical Trials: a vision of the future

Marco Viceconti

Executive Director, Insigneo institute



The
University
Of
Sheffield.

Sheffield Teaching Hospitals
NHS Foundation Trust



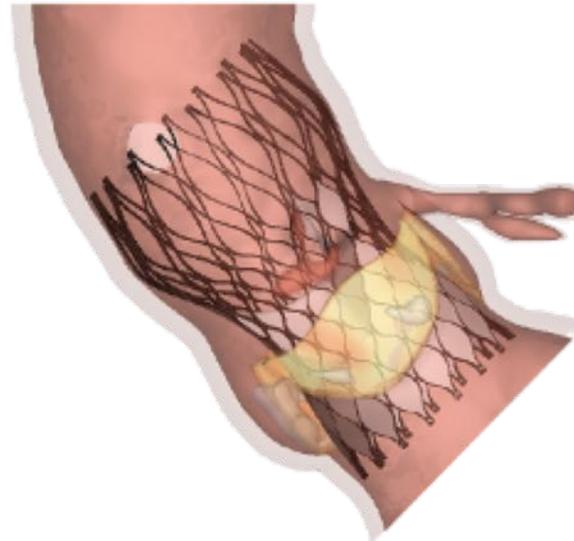
In silico: Who are the End Users?



DIGITAL PATIENT

Subject-specific predictions for decision-support, diagnosis, treatment-planning, stratification

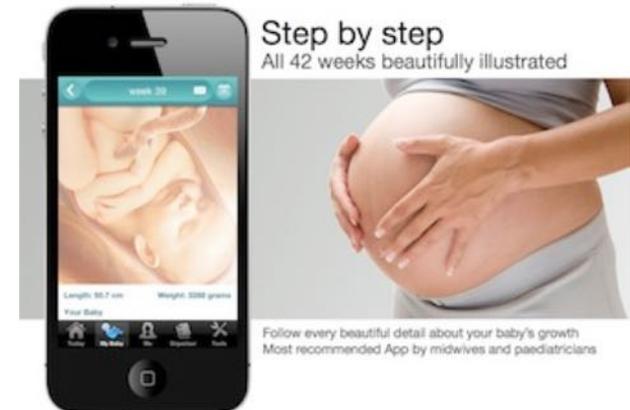
FOR THE DOCTOR



IN SILICO CLINICAL TRIALS

Virtual patient cohorts for 3R, surrogate outcomes, augmented clinical trials

FOR THE INDUSTRY



PERSONAL HEALTH FORECASTING

Subject-specific predictive models for mobile and digital health and wellness

FOR THE PATIENT - CITIZEN

De-risking medical products

Medical Products

- Pharmaceuticals
- Medical Devices
- Biologicals
- Combinatory
-

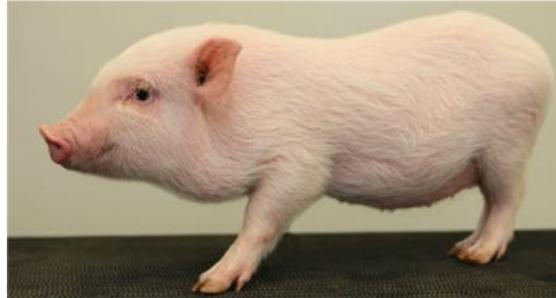
Requirements

- Cost-effectiveness
 - Risk-effectiveness
 - Safety
 - Effectiveness
- 
- Efficacy

Testing safety and efficacy



IN VITRO PRE-CLINICAL TESTS

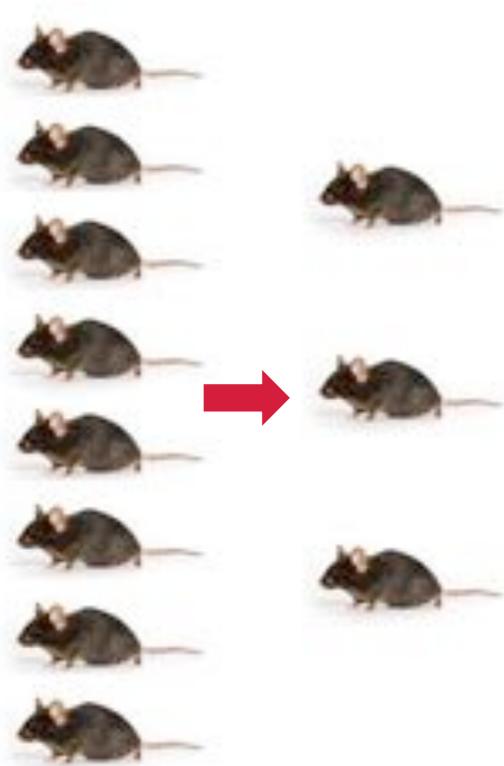


IN VIVO PRE-CLINICAL TESTS

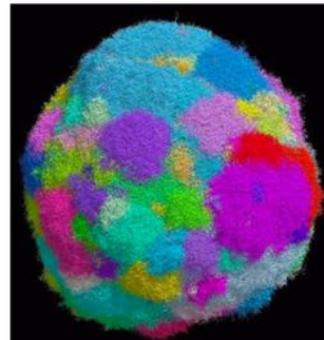
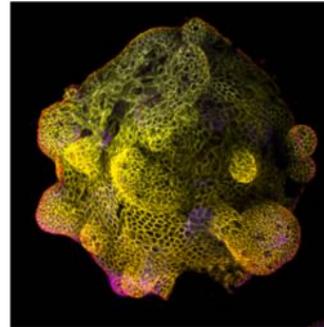


IN VIVO CLINICAL TRIALS

The role of *in silico*

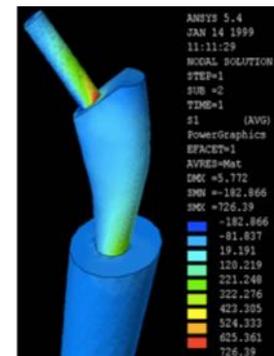


Reduce



Refine

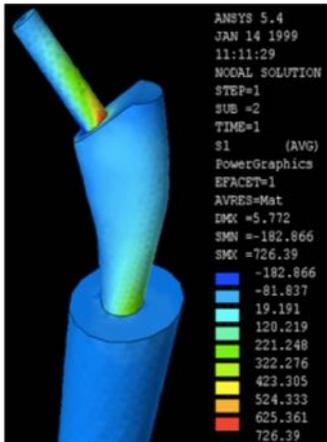
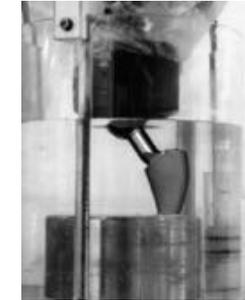
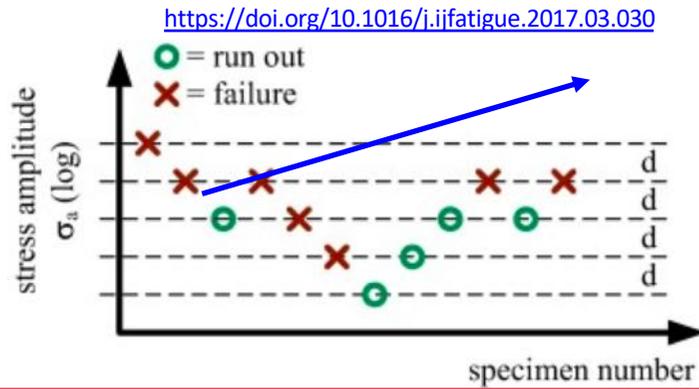
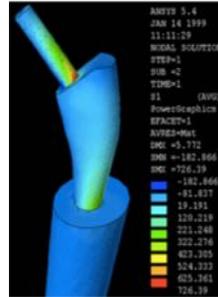
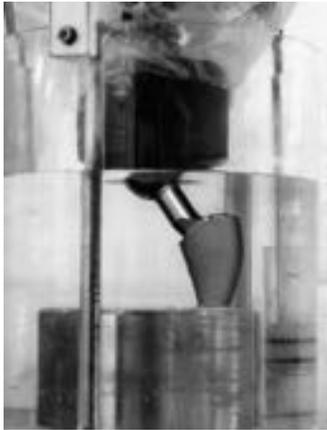
Reduce suffering
improve accuracy



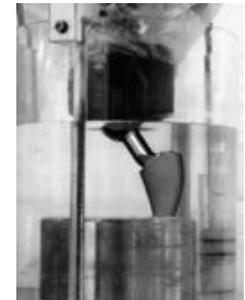
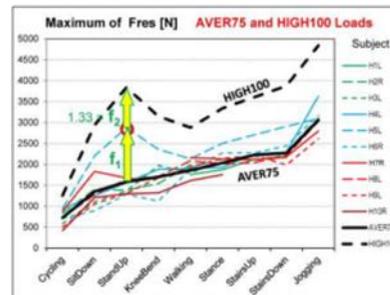
Replace

3R: in vitro tests

Reduce



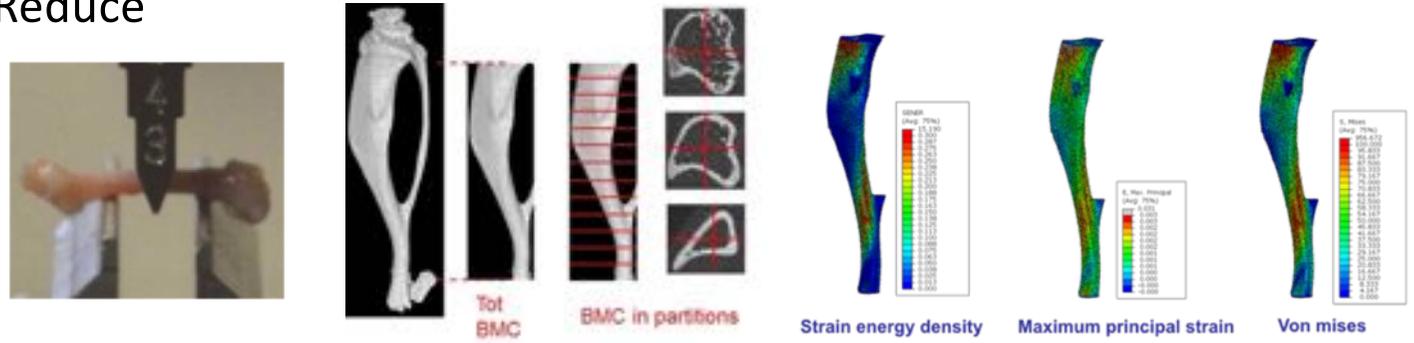
Refine



3R: animal tests



Reduce



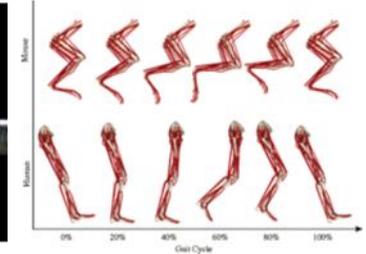
Refine Ovariectomy / Sham



<https://doi.org/10.1186/s13395-017-0143-9>

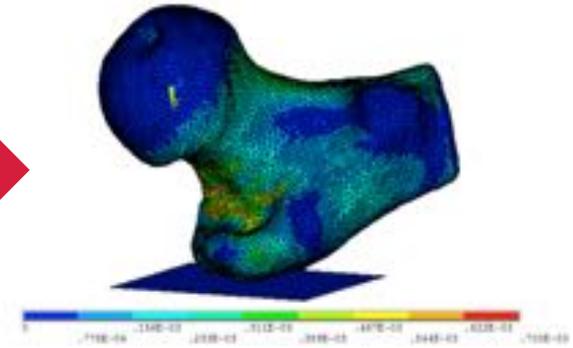


Duchenne knock-out

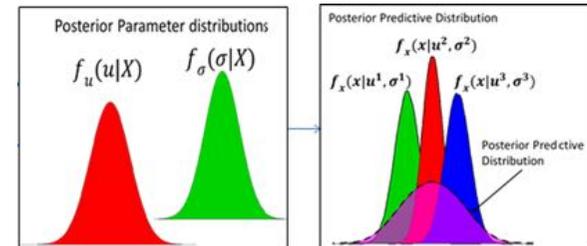
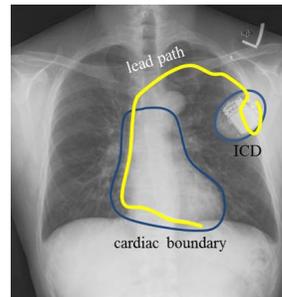


3R: clinical trials

Reduce

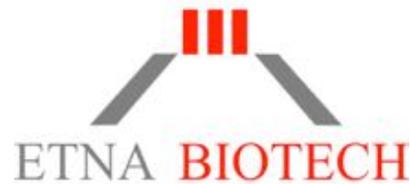


Reduce



<http://dx.doi.org/10.1016/j.res.2013.11.005>

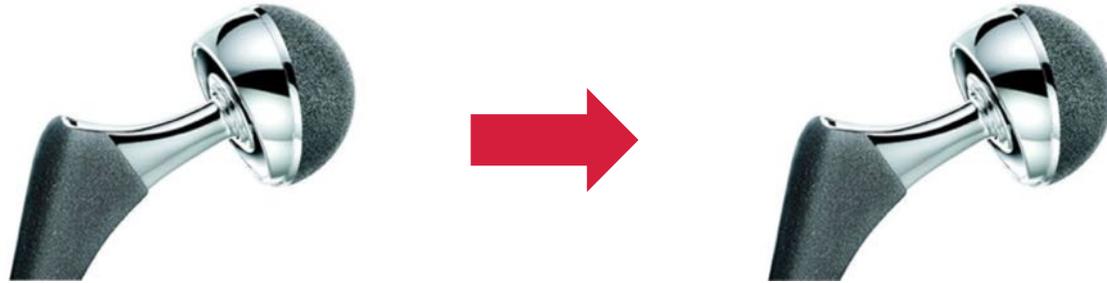
Reduce



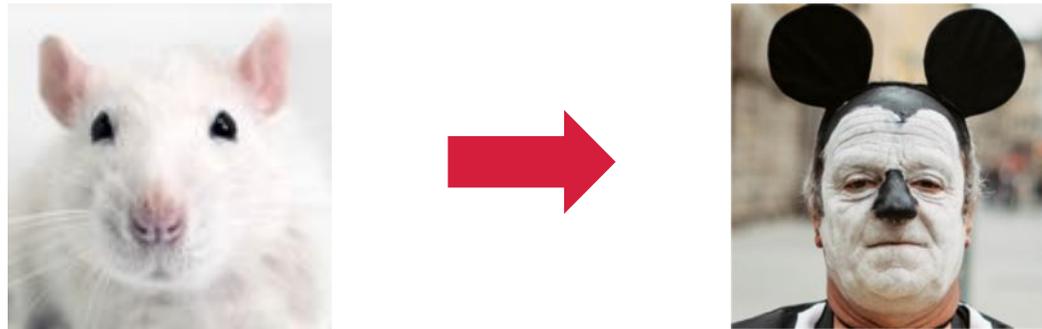
Will we ever replace?



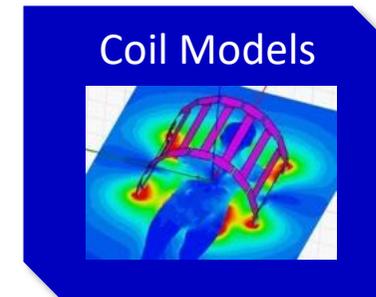
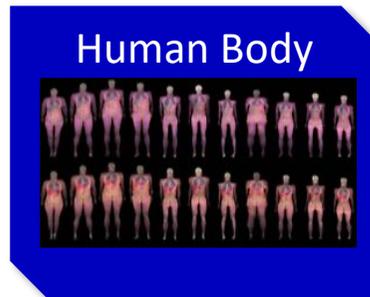
Replace



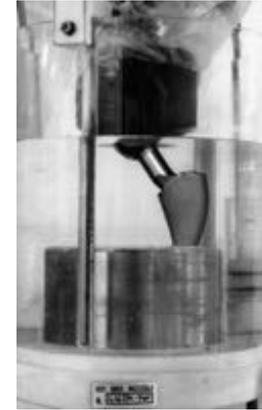
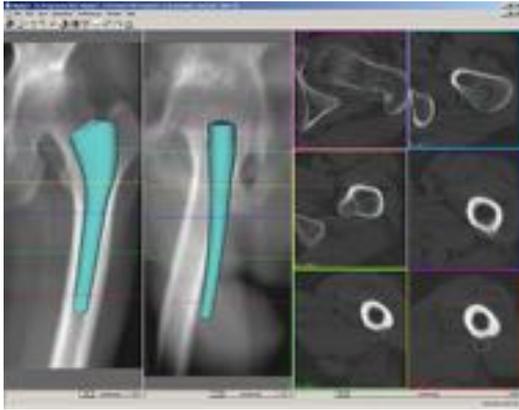
Replace



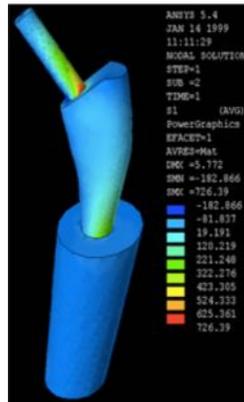
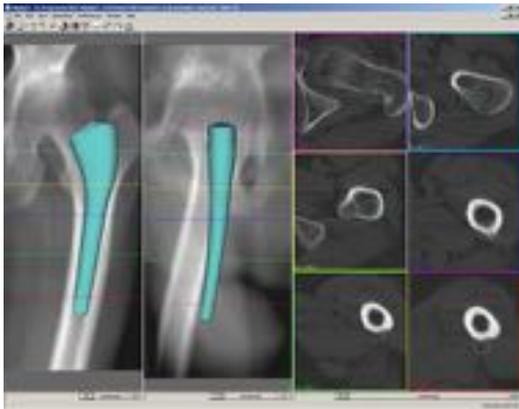
Replace



Back to the future: custom-made

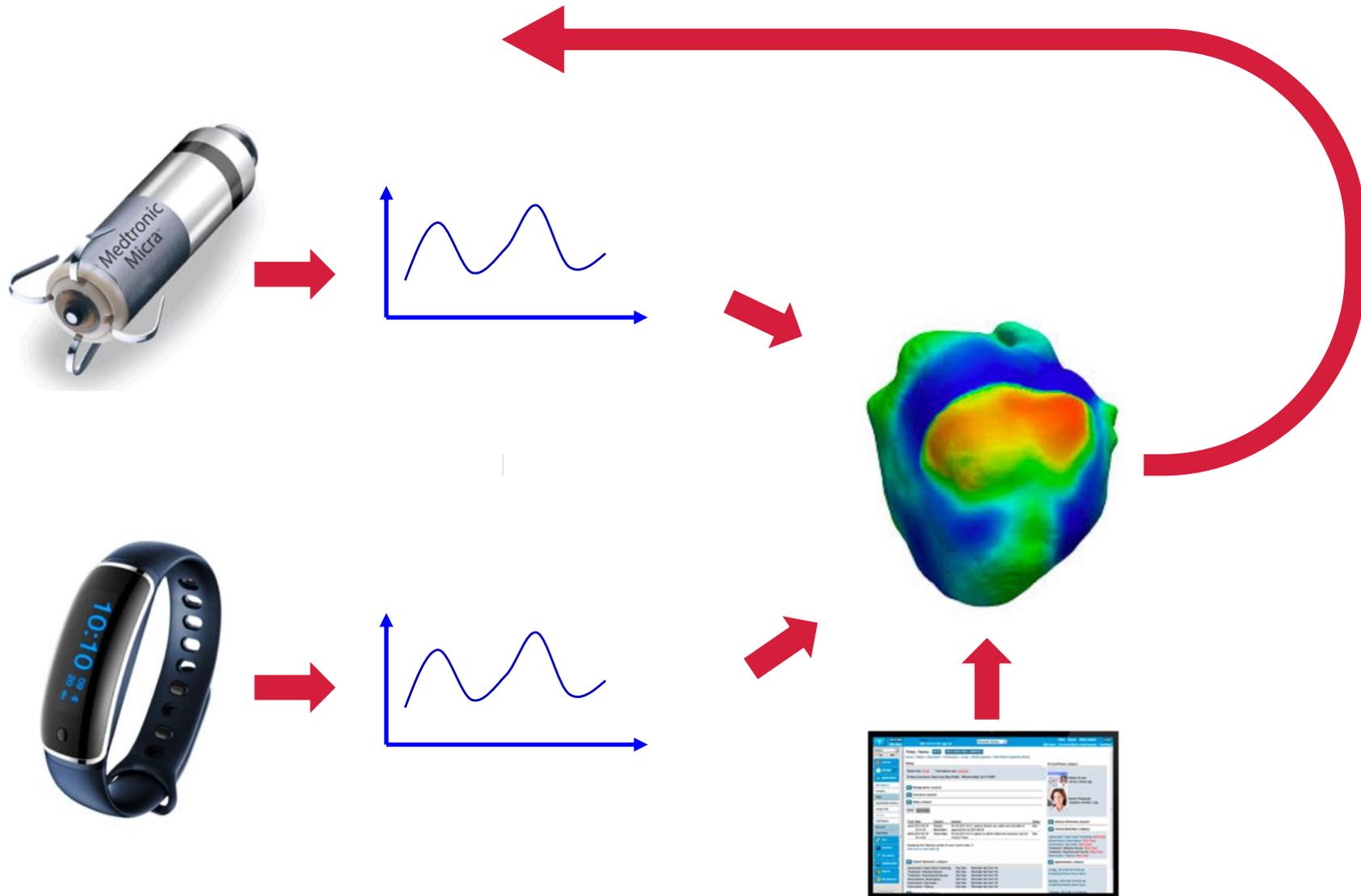


3 weeks



3 days

The Digital Twin

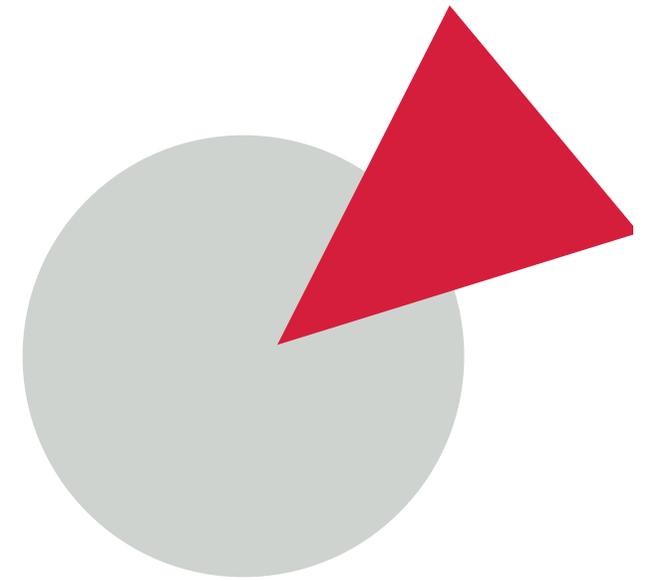


(Very) coarse summary

- Bench tests: go for refinement
 - In silico models can let you explore a broad range of operational conditions
- Animal tests: go for replacement
 - Short term we need to play nice, but in silico models are most of the time way better than animal models
- Clinical trials: go for reduction
 - Replacement is not on the horizon yet, refinement most of the time provide massive reduction
- Look for replacement opportunities
 - In some cases the currently accepted method is predicting poorly the performance in the general population

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Thank You!



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