InSilicoTrials

WHITE PAPER

Shedding light on Digital Twin, Digital Patient, Virtual Patient and Synthetic Control Arm

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Introduction

Our society was moving towards a digital lifestyle at its own healthy pace when the coronavirus pandemic struck, and this digital transition has been pushed forward with an impressive boost. Out of all the industries, there were a lot of changes in the healthcare sector, bringing new opportunities as well as challenges: other than technology, patient expectations have also taken a new rise, where solutions are now needed as soon as possible.

The most pressing challenges of the healthcare systems around the world include uneven health care access and affordability and increasing demand for services from growing populations with longer life spans. Health information and digital technologies play a significant role in overcoming these challenges by supporting population health goals, improving patients' experience, and driving insights into health conditions. [1]

The scope of this white paper is to clarify the different definitions of Digital Twin, Digital Patient, Virtual Patient and Synthetic Control Arm in the Pharma and MedTech fields.

Clarifying Concepts

What is a Digital Twin?

In simple terms a Digital Twin is a highly complex virtual model, which is the exact replica of its physical counterpart. This can be anything from a car to an industrial machinery, from an airplane to a bridge or a building and so on.

Virtual replicas of physical objects or services they represent in real time, Digital Twins allow to predict the future performance of the physical asset and to test improvements thanks to state-of-the art Modeling, Simulation and Artificial Intelligence algorithms.

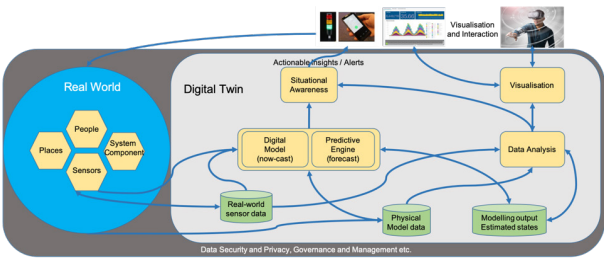

Figure 1: IBM High-level component view of a digital twin

The Digital Twin is updated in real time by the data collected from the sensors connected to the physical asset and uses simulation programs, machine learning and reasoning to provide useful information about the asset and to develop predictive models of future performance.

Digital Twins for medicine and device development

Digital Twins can improve the design, development, testing, and monitoring of new drugs and medical devices.

Drugs: Imagine having at disposal a panel of thousands drug compounds to virtually treat Digital Twin copies to predict individual risk-benefit profiles. Predictions could inform clinical trials design, enabling an effective validation of individuals and sub-groups expected to most benefit from specific drug treatments. The usage of Digital Twins thus could greatly increase the accuracy and cost-effectiveness of clinical development programs with a huge impact on both drug quality and costs.

Devices: A Digital Twin of a medical device enables engineers and designers to test the characteristics or uses of a device, evaluate alternatives in design or materials, and test the success or failure of the modifications in a virtual environment before manufacturing. This significantly reduces the costs of failures, optimizing the amount of physical testing to be conducted, and enhances the performance and safety of the final product.

What is a digital patient or the digital twin of the human body?

A Digital Patient is a personalized Digital Twin of a patient: an integrated framework of methods and technologies, updated with each measurement, scan or exam, that enables a holistic management of the patient.

It integrates all relevant medical information, and takes into account psychological, behavioral and genetic data as well. It combines scientifically proven knowledge with biophysical modeling and information obtained by processing and combining data, leveraging the power of AI and analysis.

In clinical care, the Digital Patient could be used to better predict disease course and treatment response. This would represent personalized medicine at its best: acknowledging the full array of individual disease trajectories and drug responses and ready to valorize the competitive framework of value-based healthcare.

Even Digital Twins reflecting only partial aspects of a person could considerably increase the predictive power of clinical trial outcomes and promote a shift from reactive towards more preventative healthcare. Digital Twins of the human body or individual organs represent an innovative paradigm for the personalization of healthcare.

Personalized and preventive healthcare

Like an electronic health record, a Digital Patient collates individual health information from different sources in one place.
But a Digital Patient is more than just a static digital record. It integrates and analyzes every bit of information – like a smart assistant that accompanies patients and their caregivers along the patient journey.

As it is updated over time, it provides intelligent advice to predict disease trajectory, support medical decisions and to help patients manage their disease. [2]

One fundamental difference between a Digital Twin of a device and a Digital Twin of a person (Digital Patient) is that the former starts logging data immediately and does so continuously, whereas the latter has to be compiled and matured over time.

Unlike a machine, a person is not born with a blueprint of their inner workings. A Digital Patient takes shape slowly starting from a generic, scientifically underpinned model, and elaborated upon with health data that is collected intermittently over a person's life.

Figure 2: Visual representation of a digital patient

What is a virtual patient?

In simple terms, a Virtual Patient is a modeling and simulation (M&S) component of a Digital Patient. To better understand this concept, the distinction between the Virtual Patient for pharma and Virtual Patient for Medical Devices is provided below.

A Virtual Patient within the pharma sector is understood as a computational model for which the parameters have been selected so that the model outcomes represent a (biological, physiological, pathophysiological, pharmacokinetic, pharmacodynamic, etc) process of a realistic human subject.

By resorting to in silico trials on Virtual Population, a cohort of Virtual Patients can be used to predict via simulations clinical measurements relevant to assess efficacy/safety of a therapy/ medical intervention. Another benefit of using Virtual Patients is the creation of a personalized Virtual Patient, obtained using as input patient-specific data, and providing precious insights for making diagnoses, treatment decisions and personal prognoses.

A Virtual Patient in the Medical Devices sector is understood as a computational model that represents the anatomy, (patho)physiology and/or lifestyle of one or more human subjects and their interaction with the medical device of interest.

One the benefits of Virtual Patients for Medical Devices are the patient-specific models that:

- 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.

As within pharma, using in silico trials on Virtual Population brings along a series of advantages summarized as follows:

- 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.

What is a synthetic control arm?

A Synthetic Control Arm is a computer-simulated control arm created using statistical methods that model data from virtual or real control patients.

Synthetic Control Arms are created using information that has previously been collected and can be used to replace or expand a control arm in a clinical trial. This data comes from sources including historical control data, real world data, or the generation of other data sets from other sources to serve as a comparator.

Synthetic Patient Data for Pharma refers to patient data generated from advanced computational methods, such as mechanistic modelling (Virtual Patients) and/or approaches based on machine learning/artificial intelligence.

A Synthetic Patient within the MedDev sector refers to a Virtual Patient built on synthetic data. It is a computational model that captures as many of the complexities of the original anatomical and (patho)physiological dataset, but that does not actually include any real patient data.

Challenges facing Digital Twin implementation in healthcare

Limited adoption
Digital Twin technology is not widely adopted in the clinical routine yet. The digital hospital of the future could leverage technologies that transform care delivery, patient experience, staff and operations management, bringing an overall improvement of medical care. [3]

On the other hand, even if the healthcare system use of Digital Twins increased, it is argued that it will remain expensive and not accessible for everyone. Thus Digital Twin technology could risk becoming a benefit reserved for people with higher financial capabilities.

Data quality
Artificial intelligence systems in Digital Twins learn from the available biomedical data: as the data is gathered through private companies, its quality could also not be high standard. Consequently, the analysis and representation of such data becomes problematic. That could eventually impact the models, which could also affect the reliability of the models in the diagnosis and treatment processes. [4]

Data privacy
The applications of Digital Twins require gathering more and more individual level data by healthcare organizations and insurance companies. Over time, these health organizations grasp a detailed portrait of the biological, genetic, physical, and lifestyle related information of a person. There is also the risk that such personalized data might end up in being used to benefit the company's interest instead of the individuals.

InSilicoTrials and Digital Twin Technology

Born in 2018, InSilicoTrials is a startup founded by a team of life science, cybersecurity and digital innovation experts, which aims to revolutionize healthcare through modeling & simulation. The life science industry has long faced the lengthy and costly process of developing new drugs and medical device: Digital Twin and Biosimulation are the key to cutting down time frames and costs in this area, with two trends pushing heavily in this direction: the regulatory tailwind (both the FDA and EMA are already endorsing these technologies) and the disruption the pandemic caused in pharma and Medtech R&D, paving the way to a new trial paradigm.

Our platform contains several cloud-based models which allow to predict the time-course of the disease or the effect of a drug. For instance, MS TreatSim simulates the immune system and the auto-immune response of virtual multiple sclerosis patients. With this tool it is possible to recreate Synthetic Control Arms or test different treatment options on a Virtual Patient. CTx NeutroSim and PCa GnRH Agonists Simulator predict the pharmacokinetics and pharmacodynamics of different drugs on populations of virtual cancer patients. STrhiPS (Safety Trials on human-induced Pluripotent Stem cells) simulates the effect of a drug on the action potential of a population of hiPSC-derived cardiomyocytes.

Similarly, in silico reproduction of existing standard testing allows to refine and reduce the number of physical experiments to be performed on medical devices. For example, SEV (Self-Expandable Valve) Radial Force Test (sevradial.insilicocardio.com) is a web-based virtual emulation of a bench standard test to characterize the mechanical properties of transcatheter heart valve replacements. The tool can be used to test different prototype designs before manufacturing, or to test the final device design for regulatory submission.

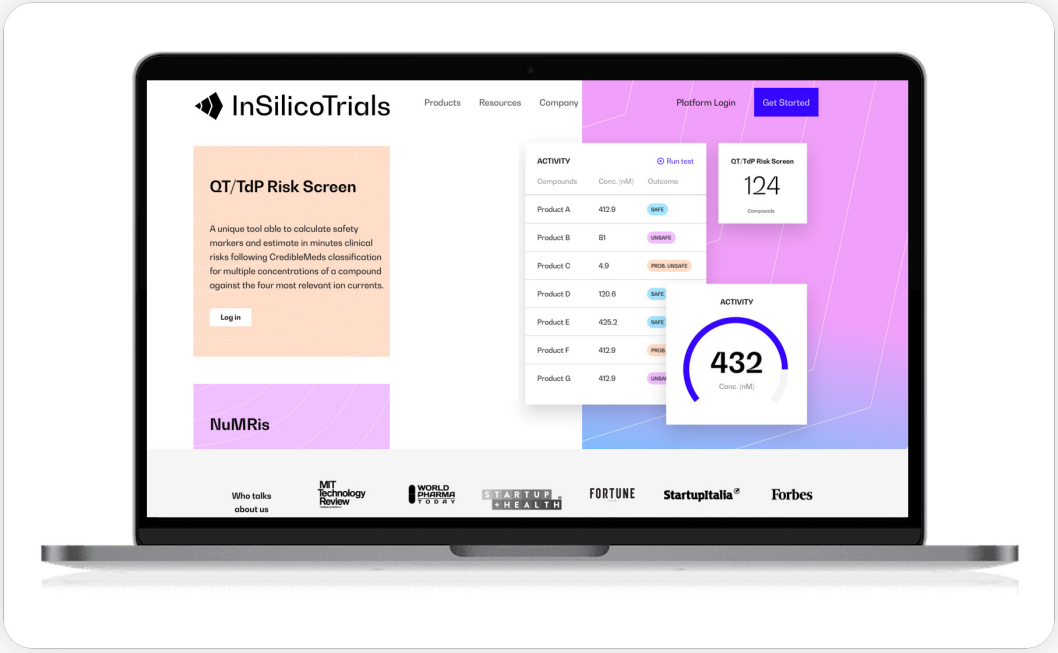

Figure 3: NuMRIs and QT/TdP Risk Screen, two example tools among InSilicoTrials' products

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