EU Horizon 2020 Research & Innovation Program
Digital transformation in Health and Care
SC1-DTH-06-2020
Grant Agreement No. 101016496

SimCardioTest - Simulation of Cardiac Devices & Drugs for in-silico Testing and Certification

SIM CARDIO TEST

Technical Report
D4.5. Demonstrator of simulation of drug effects in cellular and 3D models

Work Package 4 (WP 4)
USE CASE 3: DRUG EFFICACY & CARDIOTOXICITY

Task Lead: Beatriz Trenor, UPV, Spain
WP Lead: Beatriz Trenor, UPV, Spain

DELIVERABLE INFORMATION

Deliverable number	4.5
Deliverable title	Demonstrator of simulation of drug effects in cellular and 3D models
Description	Video of simulations performed in Use Case 3
Lead authors	Maria Teresa Mora (UPV), Beatriz Trenor (UPV)
Contributors	Sandra Pérez (UPV), Jordi Llopis (UPV), Violeta Puche (UPV), Ander Loidi (UPV), Javier Saiz (UPV), Jose María Ferrero (UPV), Lucía Romero (UPV), Maika Warita (EXC), Ilse van Herck (SRL), Hermenegild Arevalo (SRL), Samuel Baroudi (EXC), Sylvain Benito (EXC), Kévin Koloskoff (EXC)
Due date	M25
Submission date	23 January 2023
Comments	

Document history			
Date	**Version**	**Author(s)**	**Comments**
10/01/2023	V1	Beatriz Trenor	Final version
18/01/2023	V1	Delphine Feurestein	Quality Check
23/01/2023	V1	ExCom members	Validation

Table of Contents

EXECUTIVE SUMMARY

This deliverable consists of a recorded video showing the simulation workflow of Use Case 3 (UC3) to assess drug effects by means of illustrative examples. This demo shows the main characteristics of each model integrating the workflow and the main simulation outputs used to evaluate drug safety and efficacy.

The video is available on youtube and on SimCardioTest webpage.

1- INTRODUCTION

Use Case 3 (UC3) combines pharmacokinetics and electromechanical models to assess drug effects on the heart. In particular, it is focused on safety pharmacology and pharmacological efficacy in atrial fibrillation, acute ischemia, and heart failure. Numerical models and simulation software from 3 different partners are integrated in a computational workflow to simulate drug effects. The outcome of the simulations will help assess efficacy and safety from cellular to organ scale. ExactCure provides pharmacokinetic models, UPV has the know-how of the electrophysiological activity (atrial and ventricular, including pathologies), and Simula contributes to the mechanical part of cardiac simulations. A fourth partner, InSilicoTrials, is developing a tool for the whole pipeline, integrating models and software in a cloud-based platform.

2- OBJECTIVES

The objective of this deliverable is to explain through a video the fundamentals of simulation tools used by UC3 partners and to show different cases in which drug effects can be simulated and evaluated.

3- METHODOLOGIES

Among simulation tools used along drug evaluation pipeline, we can distinguish:

- The software API for pharmacokinetics developed by ExactCure.
- Electrophysiological models developed in MATLAB for unicellular simulations used by UPV.
- ELVIRA software for 3D electrophysiology used by UPV.
- SimCardEMS, a cardiac electromechanics solver, used by Simula.

4- RESULTS

The demonstration video of modeling and simulation of drug effects in cellular and 3D models is available on Youtube/SimCardioTest channel and on SimCardioTest webpage.

The video sequence represents the workflow for drug assessment. It starts with the pharmacokinetic process and is followed by electrophysiological and mechanical simulations. In the electrophysiological part, cellular models are analyzed before simulating in the organ. Among the different examples, there is a clear distinction between safety pharmacology and efficacy assessment. For efficacy, the cases under study are atrial fibrillation, acute ischemia, and heart failure.

Since tools and models are still under development, results are very preliminary and might need refinement. However, this demonstrator shows the applicability of cellular and 3D simulations to evaluate drugs for safety pharmacology and to study efficacy under diverse cardiac pathologies.

5- CONCLUSION

In this deliverable, we presented the demo of UC3 simulations to assess drug safety and efficacy.

Simulations were separately performed by each partner, but the final objective is to have all the models integrated into a cloud-based platform developed by InSilicoTrials to facilitate access to users, who can use the tool to simulate drug effects in a population of patients and obtain faster results compared to regular tests.

This project received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 101016496