COST EFFECTIVNESS ANALYSIS OF REAL AND IN-SILICO CLINICAL TRIALS FOR STENT DEPLOYMENT

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Abstract:

The global coronary and peripheral stent market size was valued at USD 5.91 billion in 2019 and is projected to reach USD 8.08 billion by 2027 and the new and innovative devices are invented and developed rapidly. In this process of developing new models of stents, one of the key phases is clinical testing on live patients. The aim of in-silico medicine is to reduce, refine and replace real clinical trials with an aim to decrease costs and time needed to perform clinical study. Within the InSilc project (funded by H2020 programme, GA 777119) the platform for designing, developing and assessing stents was developed. The intended users of platforms for in-silico clinical trials are mainly Stent Biomedical companies that develop innovative models of stents. Within the DECODE project we continued the work on cost effectiveness analysis using decision tree method for comparing in-silico and real clinical study for coronary and peripheral stent deployment.

Keywords: coronary and peripheral artery, in-silico clinical trials, stent deployment, cost effectiveness analysis, decision tree.

1. Introduction

Real clinical trials require approval by a regulatory authority and an ethics committee review of the pre-clinical regulatory submission [1]. The basic assumption is that database collected in the clinical study is a relatively small but a representative selection of subjects and the researchers have to generalise the results so they could be applicable to a larger patient population. If the sample is too constrained or poorly selected, it hinders the broad applicability of the results. This is not only a statistical concern, but also an ethical and medical one [2]. Within the InSilc project (2017-2021) an *in-silico* clinical trial platform was developed for designing, developing and assessing drug-eluting bioresorbable vascular scaffolds (BVS), by building on the comprehensive biological and biomedical knowledge and advanced modelling approaches, to simulate their implantation performance in the individual cardiovascular physiology. The platform is also applicable on the other models of stents, such as BMS, DES, peripheral stents etc. [3].

Testing of new and innovative models of vascular stents, scaffolds and balloons in real clinical trials is time-consuming, expensive and highly inconvenient for the patients included in the study. Therefore, the intention is to replace, reduce and refine a real clinical study with an in-silico clinical study and in-silico testing of the innovative models of stents in order to decrease the costs and the time required to perform a real clinical study. We analysed cost-effectiveness of using in-silico clinical trials for stent deployment in comparison with real clinical trials.

2. Method and Materials

The InSilc platform is based on the extension of existing multidisciplinary and multiscale models for simulating the drug-eluting BVS mechanical behaviour, the deployment and degradation, the fluid dynamics on a micro- and macroscale, and the myocardial perfusion, for predicting the drug-eluting BVS and vascular wall interaction in the short- and medium/long term.

The developed InSilc platform consists of different simulation modules/tools - some of which can be considered as stand-alone modules and, therefore, can be used separately if there is such demand from the targeted users. The modules integrated in the InSilc platform are: Mechanical Modelling Module, 3D reconstruction and plaque characterization tool, Deployment Module, Fluid Dynamics Module, Drug Delivery Module, Degradation Module, Myocardial Perfusion Module, Virtual Population Physiology and Virtual Population database (Figure 1). These tools are applicable to all types of coronary and peripheral stents, such as Bare Metal Stents (BMS), Drug-eluting Stents (DES) and Bioresorbable Vascular Stents (BVS). This is a great advantage of InSilc allowing it to be utilised by a wide range of users.[4]. Drug-coated balloon simulation and optimisation system for the improved treatment of peripheral artery disease has been considered in the DECODE project [5]. For the potential user, i.e. a company that develops a new model of stent, it is of key importance that cost-effectiveness analysis is performed, so the decision about the use of the real or in-silico clinical trial can be made.

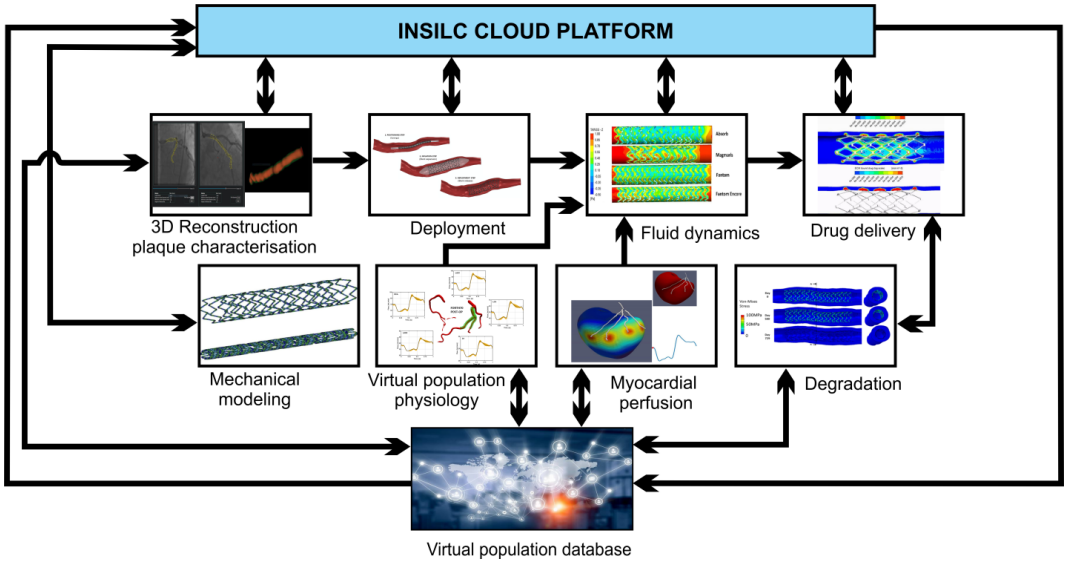

Fig. 1. InSilc cloud platform

Decision analysis and cost-effectiveness analysis are quantitative techniques that provide a systematic approach to integrating evidence within the context of a specific decision problem. We can define some steps in the decision analysis: 1) define the decision problem (including specifying the decision-maker and the ultimate goal or objective of the decision); 2) identify all the decision alternatives; 3) list all the possible outcomes of each decision alternative; 4) define the relevant time horizon; 5) map out the sequence of events leading from the initial decision to the relevant outcomes including chance events and secondary decisions; 6) quantify uncertainty: determine the probability of each chance outcome; 7) quantify values: assign a value to each outcome; 8) calculate the expected value of each decision alternative [6]. The process of explicitly quantifying the uncertainty and values involved in a decision problem provides valuable insight into the key issues and controversies inherent to the decision.

3. Results and Discussion

A *decision node*, typically represented by a square, is a point where several alternatives are possible. A *chance node*, typically represented by a circle (blue color in Figure 2), is a point in a decision tree where chance determines which event will occur. The sum of probabilities for all branches emanating from a chance node must equal 1.0 or 100%, because one of the events must occur.

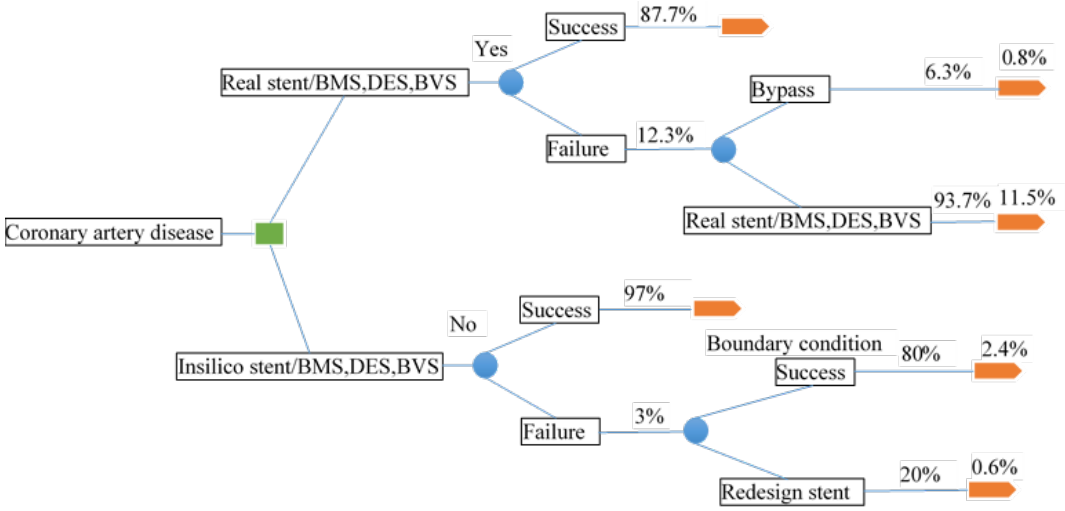

Fig. 2. Cost decision tree for in-silico and real stent (BMS, DES, BVS) trial

The cost decision tree for in-silico and real clinical trial is presented in Figure 2. Accordingly, the main decision that should be made is: real or in-silico clinical trial. We took into account Bare Metal Stents (BMS), Drug-eluting Stents (DES) and Bioresorbable Vascular Stents (BVS). The average value for success is 87.7% while failure amounts to 12.3%. Failure goes again to stent procedure 93.7% while for bypass procedure it is 6.3%. On the other site, in-silico trials give only 3% failure where 80% can be solved with change of the boundary condition and 20% requires redesign of the stent.

Conclusion

In this study, we have performed a cost-effectiveness analysis using a decision tree for Bare Metal Stents (BMS), Drug-eluting Stents (DES) and Bioresorbable Vascular Stents (BVS) deployment in the coronary and peripheral arteries. We used in-silico cloud platform developed within the InSilc project and then exploited in the DECODE project [4,5]. It has been found that in-silico trials give only 3% failure, where 80% is solved with the change of the boundary condition and 20% goes again to redesign of the stent.

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References

[1] Learn About Clinical Studies, NIH U.S. National Library of Medicine, https://clinicaltrials.gov/ct2/about-studies/learn#ClinicalTrials,
[2] Intelligent drug discovery: Powered by AI, Francesca Properzi et al., 2019. See also: https://www2.deloitte.com/ us/en/insights/industry/life-sciences/artificial-intelligence-biopharma-intelligent-drug-discovery.html
[3] H2020 InSilc project: In-silico trials for drug-eluting BVS design, development and evaluation, www.insilc.eu

[4] H2020 DECODE ITN project: Drug-coated balloon simulation and optimization system for the improved treatment of peripheral artery disease, https://www.decodeitn.eu/

[5] Fotiadis, D., Filipovic, N., In-silico trials for drug-eluting BVS design, development and evaluation, The Project Repository Journal January 2021 – Volume 8, 2021

[6] Sox H, Blatt M, Higgins M, Marton K. Medical Decision Making. 2nd ed American College of Physicians; Philadelphia: 2007