A SURROGATE MODEL OF THE THROMBECTOMY PROCEDURE FOR IN SILICO STROKE TRIALS

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Introduction

In silico trials (ISTs) consist in virtually simulating a medical procedure on a cohort of virtual patients, and aim at supporting the development and evaluation of new medical devices, procedures, or drugs, reducing the risks, time and cost of clinical trials [1]. Endovascular thrombectomy (EVT) is a minimally-invasive mechanical treatment for acute ischemic stroke, aiming at removing the thrombus occluding a cerebral artery with a stent-retriever and/or aspiration catheters. In this work, a surrogate model of the (EVT) procedure is developed and integrated in a framework to run the first proof-of-concept *in silico* stroke trials [2].

Methods

One hundred cerebrovascular anatomies were reconstructed from images of stroke patients within the INSIST European project (www.insist-h2020.eu). Thrombi of different length and composition were modeled (Fig.1A), following distributions found in stroke patients. Finite-element (FE) analyses of EVT with stent-retriever were run with the settings described in [3]. A simulated EVT procedure is successful if the thrombus is removed from the vessels, unsuccessful otherwise (Fig.1B). A geometric characterization of the vascular anatomies was performed as described in [4], and an analysis was conducted to identify the most important parameters for the determination of the virtual EVT outcomes. A total of 8 parameters (6 anatomic and 2 thrombus characteristics) were identified and chosen as inputs for the surrogate EVT model. The chosen surrogate model is a binary classifier, using a logistic regression algorithm, trained on the realizations from the FE simulations. The final model, given as input the 8 parameters describing a new patient, provides the probability of successful recanalization.

The surrogate model was integrated in an event-based framework for IST for stroke treatments, developed by INSIST partners [2]. The first step of the framework generates the virtual population of stroke patients, from which the required set of 8 input parameters is derived. The surrogate EVT model is interrogated for each virtual patient, providing population-based results on the effectiveness of the treatment. First, a *Validation trial* is run to verify the reliability of the model, by comparing the IST results with a real clinical trial [5]. Then, a *Thrombus composition trial* is run to compare the treatment outcomes in different subpopulations, followed by a *Device comparison trial* demonstrating the use of the IST for comparing the performance of different devices.

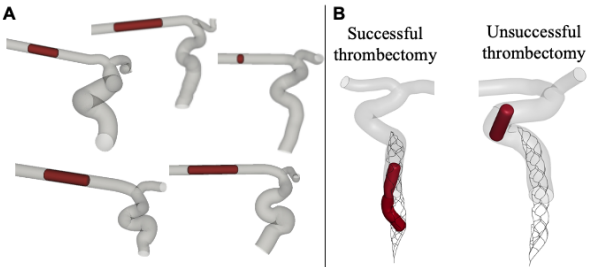

Figure1: A) Examples of cerebrovascular models. B) Successful and unsuccessful virtual EVT procedures.

Results

The *Validation trial* showed that the surrogate EVT model was able to produce a similar success-rate as the real clinical trial. The *Thrombus composition trial* reported higher success-rate for the subpopulation with soft thrombi (with high content of red blood cells), with respect to hard thrombi (rich in fibrin). The *Device comparison trial* showed improved recanalization results with a newer stent design, although these results are only exploratory as the surrogate model for the newer device lacks data for validation.

Discussion

This work presented the development of a surrogate model of the EVT procedure. The model was integrated in a framework for *in silico* stroke trials and its reliability was proven by comparison with the results of a real clinical trial with the same inclusion criteria. Two other exploratory ISTs were run, demonstrating the use of the IST platform for the selection of subpopulations for the real clinical trials, or for a preliminary assessment of the performance of new devices, which can save the costs and risks of traditional clinical trials.

References

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