Cardiovascular in-silico models for understanding and stratification of Hypertrophic Cardiomyopathy

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The complex and heterogeneous phenotype of Hypertrophic Cardiomyopathy (HCM) is not limited to only myocardial hypertrophy but includes a set of functional manifestations including the obstruction of the left ventricular outflow tract (LVOT), coronary dysfunctions, autonomic dysregulation or alteration of atrio-ventricular coupling. Within the framework of EU SMASH-HCM project, WP5 aims at proposing novel system-level mechanistic models to investigate the complex physiological mechanisms related to HCM.

A familly of integrated mechanistic models were proposed based on the coupling between i) electrophysiological smooth muscle cell (SMC), ii) the vascular systemic and pulmonary systems, iii) multi-segment ventricles, iv) LVOT and v) baroreflex regulation. These models were analysed during rest and exercice, taking into account modification of LVOT obstruction during exercice. Based on this familly of models, an original hybrid digital twin framework for HCM phenotyping, combining personalized cardiovascular models and machine learning classifier, was proposed to provide an explainable risk stratification of HCM patients.

The adaptation of the model to HCM confirmed the important influence of LVOT obstruction at the coronary microcirculatory level, and provide insights into the physiological mechanisms regulating dynamic LVOT obstruction, myocardial strains, and hemodynamics during rest and exercise. The cardiovascular model was personalized to 176 HCM patients, showing a good agreement between simulated and clinical data. By deriving biomechanical parameters from personnalized models, mechanistic phenogroups were identified and were integrated with a random forest classifier pre-trained on an independent registry, leading to a multi-layered explainable risk stratification of HCM patients. The proposed digital twin approach offers promising results toward the integration in the SMASH-HCM decission support system for explainable and personalized HCM management.