Personalised Electromechanical Model of the Heart for the Prediction of the Acute Effects of Cardiac Resynchronisation Therapy

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Abstract. Cardiac resynchronisation therapy (CRT) has been shown to be an effective adjunctive treatment for patients with dyssynchronous ventricular contraction and symptoms of the heart failure. However, clinical trials have also demonstrated that up to 30% of patients may be classified as non-responders. In this article, we present how the personalisation of an electromechanical model of the myocardium could help the therapy planning for CRT. We describe the four main components of our myocardial model, namely the anatomy, the electrophysiology, the kinematics and the mechanics. For each of these components we combine prior knowledge and observable parameters in order to personalise these models to patient data. Then the acute effects of a pacemaker on the cardiac function are predicted with the *in silico* model on a clinical case. This is a proof of concept of the potential of virtual physiological models to better select and plan the therapy.

1 Introduction

Cardiac resynchronisation therapy (CRT) involves implanting a pacemaker to improve the synchronicity of cardiac contraction. It has recently been shown to be an effective method of treating patients with dyssynchronous ventricular contraction and symptoms of heart failure. However, clinical trials have also demonstrated that up to 30% of patients may be classified as non-responders. There remains major controversy surrounding patient selection and optimisation of this expensive treatment (e.g. lead positioning, pacemaker settings). Therefore, new approaches are needed for improved patient selection and a better planning and delivery of the therapy.

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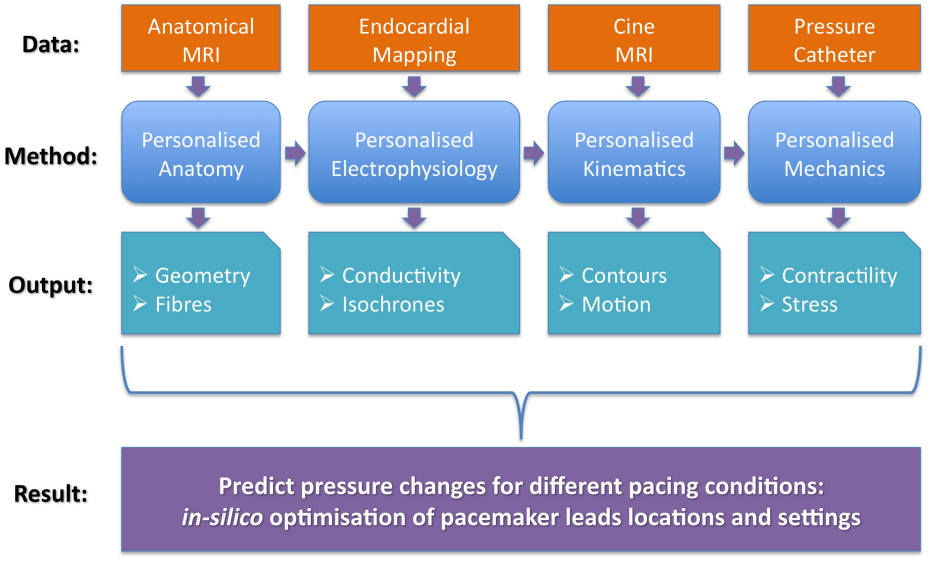

Fig. 1. Global scheme of the clinical data used for the personalised models, the generated output maps and parameters, and the resulting predictions

In this article, we demonstrate a proof of concept on a first case study of the personalisation of an electromechanical model of the heart for prediction of the changes in cardiac function due to changes in pacing (see Fig. 1). Such predictions can be used to quantify the improvement in cardiac function that can be expected from CRT and also to optimise the pacemaker implantation and settings. In this work we only focus on the acute effects of resynchronisation.

Recently, complex models have been used to simulate CRT on a generic anatomy and compared with animal experiments [1,2] which provides important insights on the pathophysiology of dyssynchrony. However, in order to translate to the clinic and impact the patient management and the therapy planning, such models need to be personalised to the specific parameters of each patient, which remains very challenging.

The proposed approach involves models whose complexity is directly related to the phenomena observed in clinical data. This is the reason why these models are often simplified compared to the very detailed models available in the literature. Involving a limited number of parameters can allow their identification from clinical measurements on a specific patient. We illustrate in this article the personalisation of several components (Fig. 1). A preliminary section details the clinical context, the data acquisition, and the data fusion. We then present the four sections concerning the personalisation of the anatomy, the electrophysiology, the kinematics and the mechanics. Finally we demonstrate this first proof of concept on the prediction of the cardiac function for two different pacing conditions.

Due to the limited space, the details of each model and their personalisation algorithms are not given in this article, but can be found in the references.

2 Clinical Context, Data Acquisition and Fusion

For cardiac modelling, the fusion of anatomical, mechanical, and electrical data is of primary importance. We use here a real-time registration solution as described in [3] that allows the spatial integration of MRI-based anatomical and functional data with X-ray-based catheter data, such as intracardiac electrical and pressure signals. The MR examination involves bSSFP Cine imaging for the estimation of ventricular function and volumes, and late enhancement images with gadolinium contrast agent for scar anatomy. The non-contact mapping is performed using the Ensite 3000 multi-electrode array catheter system (St Jude, Sylmar, CA).

The patient of this first case study is a sixty year old woman with NYHA class III symptoms (NYHA classes stand for the stages of heart failure according to the New York Heart Association. Patients with NYHA III are comfortable at rest but any other activity causes fatigue, palpitation, or dyspnea). The aetiology of heart failure is thought to be dilated cardiomyopathy although cardiac MRI did show two non-viable areas of a moderate size corresponding to the drainage area of the left anterior descending (in the apical and mid-inferoseptal segments, see Fig. 2) and of the left circumflex coronary artery (mid-inferolateral segment of the left ventricle, see Fig. 2), which are consistent with a previous subendocardial infarction. However, there was no flow-limiting disease on coronary angiography. Ejection fraction of the left ventricle was around 30% on maximal tolerated medication. The patient suffers from a left bundle branch block (LBBB). Echocardiography, including Tissue Doppler, confirmed significant mechanical dysynchrony in keeping with the ECG findings, with in particular a QRS duration of 144 ms.

3 Personalised Anatomy

3.1 Myocardial Shape

There is an important literature on the segmentation of the heart from medical images. However, to cope with extreme and variable anatomies due to pathologies, we developed a simple yet efficient method which combines specific image processing tools to extract the biventricular myocardium from Cine-MRI. The approach is made of three steps: 1) image preparation, in order to enhance image quality; 2) interactive segmentation of the myocardial boundaries at mid-diastole; and 3) construction of the volumetric anatomical model. For regional personalisation of the simulation, each tetrahedron is automatically labelled according to the anatomical region it belongs to (LV+septum, RV, scar tissue, see Fig. 2). The scar label is based on the expert manual delineation on late enhancement MRI.

3.2 Cardiac Fibre Orientation

The complex fibre architecture has an important role in the electrical and mechanical functions of the heart. We use the statistical atlas of the cardiac fibre

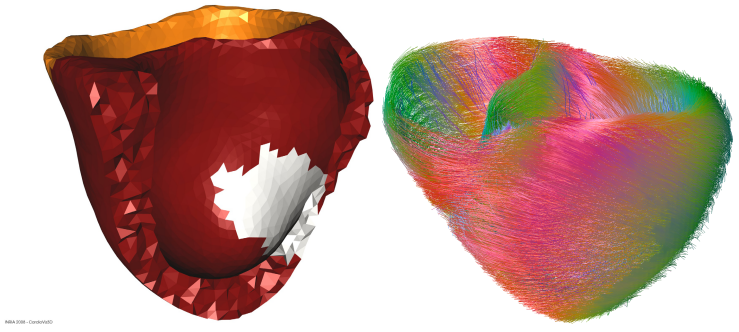

Fig. 2. (Left) 3D anatomical model of patient myocardium: left ventricle *(in red)*, right ventricle *(in orange)* and scar *(in white)*. (Right) personalised muscle fibres from registered atlas.

architecture and the methodology described in [4]. This atlas was computed from a population of *ex vivo* canine hearts but was shown to be consistent with human hearts. We first globally align the atlas with the patient's heart using a constrained affine registration. Then, a non-linear registration algorithm is performed. The resulting deformation field is used to resample and reorient the atlas of DT-MRIs to fit the patient geometry.

4 Personalised Electrophysiology

Clinical electrophysiologic data currently available only reliably describe the depolarisation times, and not the extracellular or transmembrane potentials. So we chose the Eikonal electrophysiology model accordingly. The Eikonal equation is static, and the front can be observed at a larger scale, resulting in much faster computations. An anisotropic multi-front fast marching method was developed in order to solve the Eikonal model equations very efficiently. We base our model on the Eikonal diffusion (ED) equation [5].

To personalise this electrophysiology model, there are two important adjustments to perform: the onset of the electrical propagation, and the local conduction velocity. To adjust the electrical onset, we use the earliest activation from the Ensite map. For the conduction velocity, we estimate it in the Eikonal model by matching the simulated propagation times of the model to the clinically measured propagation times of the patient. An automatic adjustment method of the apparent conductivity (AC) has been designed for surfaces [5]. We currently use a manual adjustment in order to extrapolate this to the volumetric model, in order to obtain isochrones within the muscle and in the right ventricle.

5 Personalised Electromechanical Models

The myocardium constitutive law is active, non-linear, anisotropic, incompressible and visco-elastic. Numerous laws were proposed in the literature, see e.g.

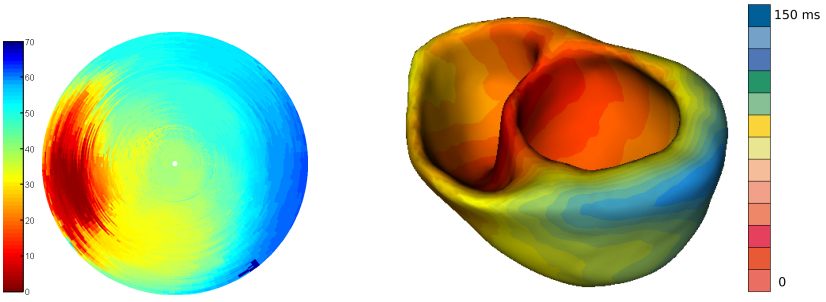

Fig. 3. (Left) LV endocardium Ensite isochronal map in sinus rhythm (in ms), (Right) simulated volumetric isochrones for extrapolation of endocardial data

[6,7,8,9,10] and references therein. The models used in our study were designed to have a complexity compatible with the clinical data used for the personalisation.

We use two different electromechanical models for the muscle contraction, depending on the application. We first introduce a simplified model as a deformable model in order to extract the motion and contours from the dynamic images (Personalised Kinematics, Subsection 5.1). We then use this information with additional pressure data in order to personalise a more complex model of the myocardial mechanics, which allows to adjust contractility and estimate pressures (Personalised Mechanics, Subsection 5.2). These models are detailed in [11] and [12]. To carry out simulations, additional needs are Windkessel models and valve laws to represent the blood flows and adequate finite element and energy-preserving time discretisation strategies.

5.1 Personalised Kinematics

In this subsection, we outline a deformable model approach to estimate the motion of the heart using Cine-MRI data and an electromechanical model. The model used here is a pro-active deformable model designed for cardiac image analysis and simulation [11]. This approach consists of adding image forces to the vertices belonging to the surface of an electromechanical model. This method is related to a sequential data assimilation approach [13], as detailed in [14]. Fig. 4 shows the MR images at end-systole. The superimposed lines represent the endocardial and epicardial surfaces of the estimated mesh. Colours correspond to the intensity of the images forces.

We can observe that despite the limited quality of routine clinical images, the estimation of the myocardial contours is relatively good, especially for the left ventricle. Due to the lack of contrast on the epicardium and the small thickness of the right ventricle, achieving a good dynamic segmentation of the RV is still very challenging. Finally, even if Cine-MRI only shows the radial motion, this

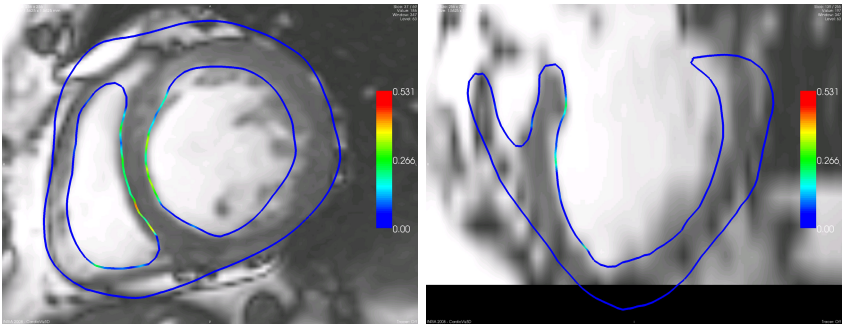

Fig. 4. Results of the motion tracking: delineation of the estimated mesh superimposed with Cine-MRI at end-systole in short- and long-axis views. Colour encodes the intensity of the image forces (blue: small, red: large).

approach estimates a complete 3D motion, interpolating with the electromechanical model for the circumferential and longitudinal motion.

5.2 Personalised Mechanics

We use this estimated motion to personalise the mechanical parameters of a more complex model, in particular to ensure a realistic simulation of the stresses. The model used here, and detailed in [12], was built from a physiological point of view and is consistent with essential thermomechanical requirements (energy balances in particular), preserved from the continuous dynamical equations to the discrete versions used for simulations. We demonstrate here that the personalisation steps presented above and a proper calibration of the mechanical parameters using the pressure-volume indicators can already provide satisfactory predictability in the direct simulation of the cardiac function.

In order to take into account the infarct, the scar tissue (segmented in the anatomical personalisation) has contractility parameters decreased by a factor of 5. We then obtained a simulated motion relatively close to the one from the personalised kinematics. While there are still discrepancies, the general behaviour is very similar. However, the automatic adjustment of local parameters is needed in order to be able to improve the fitting. The work in progress on this automatic identification is very promising [15,13]. This personalised mechanical model produces simulated pressure in very good agreement with the catheter measurement in systole (see Fig. 5, Left). Note that the slope of the simulated pressure curve is not very accurate in the diastolic phase. Although this could be adjusted by changing the parameter corresponding to active relaxation, the slope is also highly affected by the synchronicity of the repolarisation wave. As the repolarisation wave cannot be effectively detected in the measurements, due to the small amplitude and gentle slope of the T wave, we instead used action potential durations based on the ECG. This of course does not accurately represent the synchrony of repolarisation, hence we did not seek the calibration of

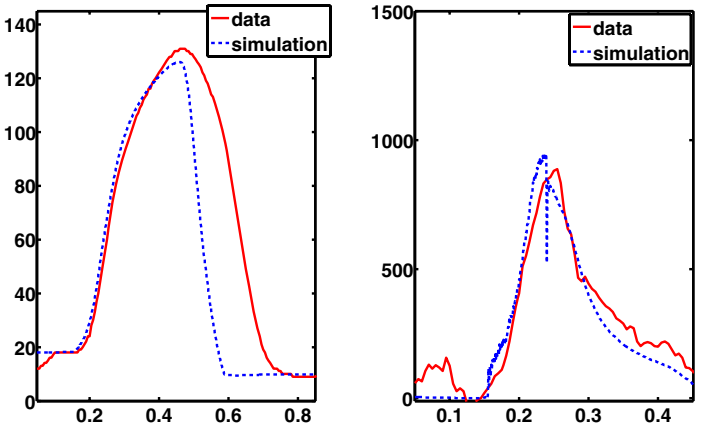

Fig. 5. (Left) Measured (solid red) and simulated (dashed blue) left ventricular pressure curves (in mmHg) in sinus rhythm (time in s). (Right) Measured (solid red) and simulated (dashed blue) left ventricular dP/dt curves (in mmHg/s) during systole in sinus rhythm (time in s).

the diastolic pressure slope. This is the reason why we only show the systolic phase in the dP/dt curves (see Fig. 5, Right).

6 Prediction of the Acute Effects of Pacing

During the electrophysiology study, different pacing conditions are tested to evaluate the effect of different pacing lead locations and delays. In this section, we test the ability of our personalised electromechanical model of the myocardium to predict the changes in the heart for two different pacing conditions. First, we simulate atrial pacing, by using ventricular isochrones similar to sinus rhythm but with a higher heart rate. We also test biventricular pacing with simultaneous endocardial left ventricular pacing (called here P1TRIV). We use the actual Ensite mapping of this pacing case to adjust the volumetric isochrones, incorporating the location of the pacing electrodes from the XMR registration.

Then, we use the mechanical model personalised in section 5.2, without changing any parameter. We input the new electrical command corresponding to the atrial and P1TRIV pacing and observe the resulting simulated pressure curves (see Fig. 7, Left), allowing to test in particular predictions on the slope of this pressure during isovolumetric contraction. As this is the major cardiac phase that is sought to be optimised by CRT, we mainly focus on the model predictive power during this phase, and early ejection. When simulating the atrial and P1TRIV pacing with the model personalised from baseline measurements, we observe a very good agreement of the pressure curve with the recorded data

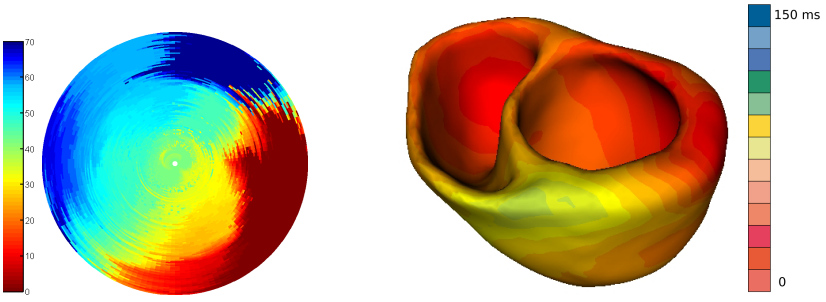

Fig. 6. (Left) LV endocardial Ensite isochronal map for P1TRIV pacing (in ms), (Right) simulated volumetric isochrones for extrapolation of endocardial data

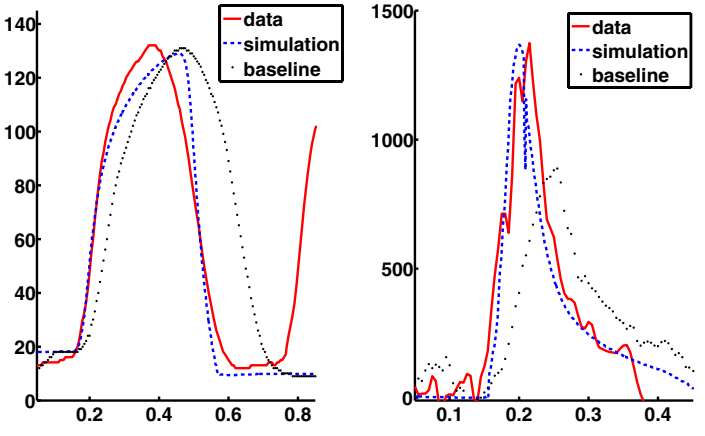

Fig. 7. (Left) Measured (solid red) and simulated (dashed blue) left ventricular pressure curves (in mmHg) with P1TRIV pacing along the cardiac cycle (time in s). (Right) Measured (solid red) and simulated (dashed blue) left ventricular dP/dt curves (in mmHg/s) during systole (time in s) with P1TRIV pacing. Baseline measurements are the dotted line.

from the pressure catheter, and the dP/dt curve is also very similar (see Fig. 7, Right, for the P1TRIV case).

One important index of the effectiveness of the contraction is the maximum of the pressure time-derivative, $(dP/dt)_{max}$. It describes how the pressure builds up during the isovolumetric contraction.

$(dP/dt)_{max}$ in $mmHg/s$	Sinus Rhythm	Atrial Pacing	P1TRIV
Measured	**930**	**950**	**1381**
Simulated	**950**	**980**	**1370**

We can see that the improvement of the cardiac function brought by the two different pacing conditions is well predicted by the *in silico* simulations.

7 Conclusion

We presented the personalisation of a complete electromechanical model of the myocardium using XMR interventional data and how this personalised model could be used to predict the effects of therapy. This model has been tested on the left ventricular pressure resulting from different depolarisation maps. The behaviour of the model in sinus rhythm as well as the predictions of the model under two pacing conditions compare well with the measured data, which make such an approach very promising. This is the first case study demonstrating how models of the heart can be adjusted to be patient-specific and a first proof of concept of how this approach can be useful for planning of therapy.

While several steps still require interactive adjustment, the methodology for automatic parameter estimation is becoming available [15,13,5]. In the case of CRT, such predictions could help optimise the pacemaker settings *in silico*, which may include the pacing lead locations and delays between chamber stimulation.

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