Personalised Biophysical Model to Optimize Left Ventricle Pacing Location for Cardiac Resynchronisation Therapy over Time

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Abstract

Cardiac Resynchronisation Therapy (CRT) causes changes in cardiac anatomy, electrophysiology and mechanics of the heart after 3-6 months of treatment. Multi-pole pacing (MPP) and multi-vein pacing (MVP) are new technologies that offer the ability to change the location of the pacing site post implant, however, the long term benefits of shifting the left ventricle (LV) pacing site are still uncertain. A personalised biophysical electro-mechanical model of a patient's heart was developed from MRI, echocardiogram, ECG and pressure catheter recordings, before and after sustained CRT treatment. Simulations of biventricular pacing of the heart were performed for 49 pacing sites across the LV free wall, in the model of the patient prior to- and after sustained pacing. The optimal region for LV pacing was determined by the acute haemodynamic response (AHR). After sustained CRT treatment the heart remodels and the models predict that the optimal region for pacing the LV would expand by 46% after this remodeling. The expansion in the optimal LV pacing region after remodeling predicts that if LV lead location was placed within the optimal region prior to CRT treatment, it will remain within the optimal region after sustained pacing.

1. Introduction

Cardiac Resynchronisation Therapy (CRT) is one of the few effective treatments for patients with drug refractory dyssynchronous heart failure, however 30% of patients fail to respond to this treatment [1]. Many factors can lead to non-response, including suboptimal LV pacing lead location [2].

In CRT, the heart is implanted with pacing leads in the right and left ventricles with the aim to resynchronise the ventricular contraction of the heart [3]. The left ventricular (LV) lead is typically implanted via the venous branches of the coronary sinus to electrically stimulate the LV epicardium. To improve the response rate of patients, the optimal location from which to pace the LV free wall has therefore received some interest. In earlier studies, it was found that the optimal location from which to pace the LV is in the non-ischemic, non-apical, postero-lateral/lateral regions of the LV epicardium, or the latest point of mechanical or electrical activation [4-6].

The heart remodels in response to sustained pacing with regards to the anatomy, mechanics and electrophysiology properties [7, 8]. New pacing catheter technologies such as multipole pacing (MPP) and multi-vein pacing (MVP) allow for the LV lead position to be altered post implant without further surgery. The long term benefits of MVP and MPP depend on whether the optimal location for LV pacing changes after remodeling due to CRT.

2. Methods

A male patient with standard indication for CRT (NYHA class III, QRSd≥120ms, LBBB on surface ECG, LV EF≤35%) was recruited and clinical data was acquired before and after six months of sustained CRT. The heart was implanted with three leads, one at the high right atria to regulate the heart rate, one at the RV apex and with a MPP LV lead in the posterior/lateral regions of the heart to synchronize ventricular contraction.

Prior to CRT implantation, 3D whole heart MR images were acquired and after device implantation, the heart anatomy was captured using 2D and 3D echocardiography. Gadolinium enhanced MR images were also acquired prior to implantation to determine the regions of infarcted tissues in the heart.

Electrical activation of the heart was measured using 12-lead ECG and invasive electroanatomical mapping of the left ventricle. At time of implant and after at least six months of sustained pacing, invasive pressure measurements were taken from the left ventricle cavity under biventricular pacing (DDD-BiV) and with baseline pacing (AAI), while X-ray fluoroscopy images were acquired. The relative change of the maximal change in pressure due to pacing, the acute hemodynamic response

(AHR), was used as a measure of the response of the heart to being paced:

$$AHR = \frac{max\frac{dP}{dt}_{DDD-BiV} - max\frac{dP}{dt}_{AAI}}{max\frac{dP}{dt}_{AAI}}$$

A Biophysically based model was used to simulate the changes in the geometry, electrophysiology, passive and active mechanics, and pressure boundary conditions of the heart before and after sustained pacing.

The geometric changes in the heart were modeled by segmenting the ventricular surfaces from MR images prior to implant [Figure 1] or echocardiographic images after at least six months of sustained pacing. Patient specific meshes were fitted to the segmentations for the patient at the two time points, before and after sustained pacing. Regions of scar tissue were segmented from gadolinium enhanced MR images and mapped to the meshes [9]. Rule-based fiber orientations, based on cadaveric and canine data, varying along the transmural, apical-basal and between the left and right ventricles were assigned to the meshes as previously described in [10].

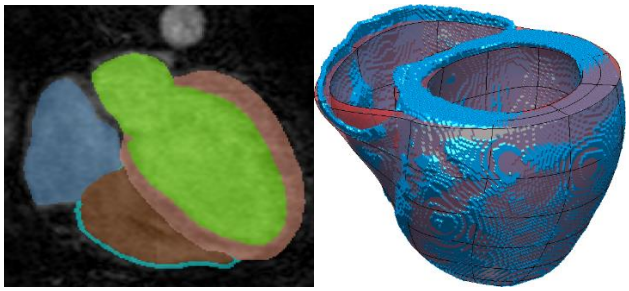


Figure 1: Models were created from the segmentation of medical images and personalized to the clinical data for the patient before and after six months of sustained pacing.

The electrical activation of the heart was simulated using CARP [11]. The location of the pacing leads on the patient meshes were modeled based on the image registration of the X-ray and MR images [12]. The patient model was personalized by fitting the time taken for the electrical activation over the ventricles to the QRS duration measured before and after sustained pacing with AAI and/or DDD-BiV pacing [9].

The passive mechanics of the heart were modeled using a transversely isotropic hyper-elastic material law. The active mechanics of the heart were modeled using a length-dependent model[10]. The systemic blood flow and boundary conditions were modeled using a three element Windkessel model. The active and passive mechanic parameters of the biophysically based models were fit to both the pressure volume relation and the AHR [10]. The models were then qualitatively validated using cine MR images.

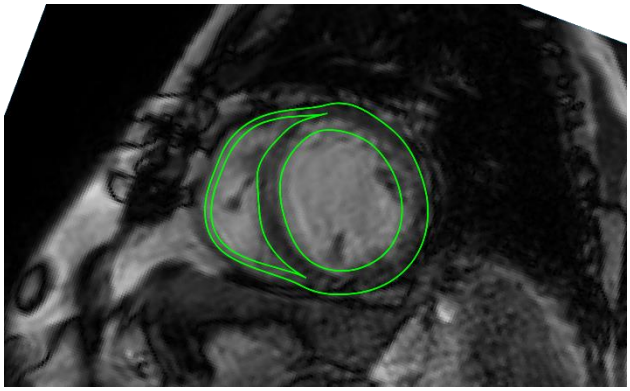


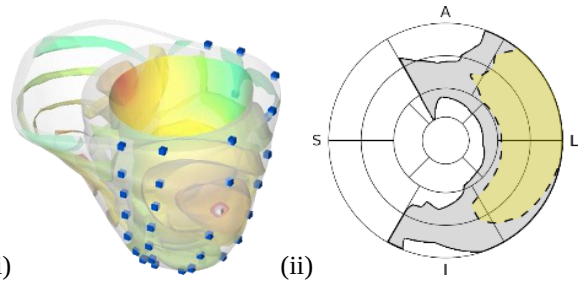
Figure 2: The model simulations (green outline) were validated using the cine MR images.

To assess the optimal pacing location on the LV free wall, the heart models were paced at 49 points on the LV epicardium. For each pacing site, the electrical activation for biventricular pacing was simulated across the ventricles. The timing of the electrical activation were then used to stimulate the contraction of the heart in the mechanic models. The AHR for the heart for being paced at the different pacing sites in the LV epicardium was calculated for the different pacing locations and interpolated across the LV free wall. The optimal pacing region was taken to be regions within 70% of the maximal AHR value [13].

3. Results

After the models were personalized to the two time points, the biophysically based model was used to predict the response of the patient to biventricular pacing, where the location of the LV pacing site was set to be 1 of 49 different pacing sites across the LV epicardium. The LV and RV pacing sites were active simultaneously and the AHR was predicted for each LV paced location, this was then used to predict the optimal area in the LV free wall from which to pace the LV.

The simulations predicted that the optimal LV pacing site the time of implant lay in the lateral region of the LV free wall, consistent with previous studies. The optimal region for pacing expanded over time with sustained pacing, increasing the coverage of the LV wall by 46% with the optimal area at time of implant persisting over time as shown in Figure 3.



(i) (ii)

Figure 3: (i) The model was paced from the LV at 49 sites across the LV epicardium. (ii) The AHR for each pacing site was mapped and interpolated on a 16 segment AHA model. The optimal LV location from which to pace the heart before (yellow) and after six months of sustained pacing (grey) was predicted for the patient case study.

Conclusions

Biophysically based models of the heart were personalized to a patient case study to model the changes in the heart before and after sustained CRT. The models were then used to simulate the response of the heart to pacing at different locations across the LV epicardium.

The models predicted that the optimal region to pace the LV in the heart at time of implant was in the non-apical lateral region of the LV, consistent with earlier studies of optimal LV pacing lead location [13]. The models predicted that the optimal LV pacing region expands over time as the heart remodeled with CRT treatment.

References

[1] E. S. Chung, A. R. Leon, L. Tavazzi, J. P. Sun, P. Nihoyannopoulos, J. Merlino, *et al.*, "Results of the predictors of response to crt (prospect) trial," *Circulation*, vol. 117, pp. 2608-2616, 2008.

[2] W. Mullens, R. a. Grimm, T. Verga, T. Dresing, R. C. Starling, B. L. Wilkoff, *et al.*, "Insights From a Cardiac Resynchronization Optimization Clinic as Part of a Heart Failure Disease Management Program," *Journal of the American College of Cardiology*, vol. 53, 2009.

[3] E. S. Chung, A. R. Leon, L. Tavazzi, J.-P. Sun, P. Nihoyannopoulos, J. Merlino, *et al.*, "Results of the Predictors of Response to CRT (PROSPECT) trial," *Circulation*, vol. 117, 2008.

[4] F. Zanon, E. Baracca, G. Pastore, C. Fraccaro, L. Roncon, S. Aggio, *et al.*, "Determination of the longest intrapatient left ventricular electrical delay may predict acute hemodynamic improvement in patients after cardiac resynchronization therapy," *Circulation. Arrhythmia and electrophysiology*, vol. 7, 2014.

[5] F. Z. Khan, M. S. Virdee, S. P. Fynn, and D. P. Dutka, "Left ventricular lead placement in cardiac resynchronization therapy: Where and how?," *Europace*, vol. 11, 2009.

[6] C. Ypenburg, R. J. van Bommel, V. Delgado, S. a. Mollema, G. B. Bleeker, E. Boersma, *et al.*, "Optimal Left Ventricular Lead Position Predicts Reverse Remodeling and Survival After Cardiac Resynchronization Therapy," *Journal of the American College of Cardiology*, vol. 52, 2008.

[7] T. Aiba, G. G. Hesketh, A. S. Barth, T. Liu, S. Daya, K. Chakir, *et al.*, "Electrophysiological consequences of dyssynchronous heart failure and its restoration by resynchronization therapy," *Circulation*, vol. 119, 2009.

[8] P. Søgaard, H. Egeblad, W. Y. Kim, H. K. Jensen, A. K. Pedersen, B. Ø. Kristensen, *et al.*, "Tissue doppler imaging predicts improved systolic performance and reversed left ventricular remodeling during long-term cardiac resynchronization therapy," *Journal of the American College of Cardiology*, vol. 40, 2002.

[9] A. Crozier, B. Blazevic, P. Lamata, G. Plank, M. Ginks, S. Duckett, *et al.*, "The relative role of patient physiology and device optimisation in cardiac resynchronisation therapy: A computational modelling study," *Journal of Molecular and Cellular Cardiology*, 2015.

[10] S. A. Niederer, G. Plank, P. Chinchapatnam, M. Ginks, P. Lamata, K. S. Rhode, *et al.*, "Length-dependent tension in the failing heart and the efficacy of cardiac resynchronization therapy," *Cardiovascular research*, vol. 89, 2011.

[11] S. Niederer, L. Mitchell, N. Smith, and G. Plank, "Simulating human cardiac electrophysiology on clinical time-scales," *Frontiers in physiology*, vol. 2, 2011.

[12] M. V. Truong, A. Aslam, C. A. Rinaldi, R. Razavi, G. P. Penney, and K. Rhode, "Preliminary investigation: 2D-3D registration of MR and X-ray cardiac images using catheter constraints," in *CI2BM09-MICCAI Workshop on Cardiovascular Interventional Imaging and Biophysical Modelling*, 2009, p. 9 pages.

[13] R. H. Helm, M. Byrne, P. a. Helm, S. K. Daya, N. F. Osman, R. Tunin, *et al.*, "Three-dimensional mapping of optimal left ventricular pacing site for cardiac resynchronization," *Circulation*, vol. 115, 2007.

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