Simulation Analysis of Mechanical Properties of the Canine Heart with Bundle Branch Block Based on a 3-D Electromechanical Model

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Abstract

Asynchronous electrical activation, induced by bundle branch block (BBB), can cause reduced ventricular function. However, effects of BBB on the mechanical function of heart are difficult to assess experimentally. Based on an electromechanical canine heart model developed recently, the mechanical properties of complete LBBB and RBBB were simulated. The geometries and myofibre orientations of ventricles were constructed based on MR scan and diffusion tensor MRI datasets. The electrical activation sequences were simulated by solutions of reaction-diffusion equations and myocardial active forces were used to calculate ventricular wall deformation based on FEM method. The results showed that there is an asynchronous contraction of the septum in BBB during systole, the ejection fraction of left ventricle during LBBB and RBBB is 21.7% and 24.7% respectively, and patients with LBBB may have a more decreased stroke volume and thus are more likely to develop cardiovascular diseases.

1. Introduction

Bundle branch block is a common complication of dilated cardiomyopathy that afflicts millions of patients in the world. Asynchronous electrical activation, induced by conduction abnormalities, can cause reduced ventricular function. However, effects of BBB on the mechanical function of heart are difficult to assess experimentally. Computer modeling may be a substitute of experiments, which can freely simulate heart in various pathological conditions. In the past decades, many mathematical models have been developed to investigate cardiac properties during BBB, but mainly focused on the electrophysiological properties of BBB [1-3]. The mechanical function of BBB has not been well investigated so far.

Usyk et al. [1] developed a three-dimensional computational model of dilated failing heart with left bundle branch block (LBBB), converged with only 48 tricubic Hermite elements to simulate passive inflation and active contraction and 768 tricubic Hermite elements to simulate electrical impulse propagation. In the study of Kerckhoffs et al. [2], the increased inhomogeneity in the left ventricle by pacing was investigated, but the geometry was represented by a simple thick-walled, truncated prolate ellipsoid and fictive fiber orientations. All these models neglected the analysis of myocardial stress, which is important for clinical diagnosis. Based on a newly developed electromechanical model of canine heart, the mechanical properties of complete LBBB and RBBB (right branch bundle block) were simulated.

2. Materials and methods

2.1. Heart geometry

The geometries of left ventricle (LV) and right ventricle (RV) were derived from Magnetic Resonance (MR) scan of an intact canine heart at the Duke University Medical Center for In Vivo Microscopy (see Figure 1A, B). The spatial discrete matrix size of the original data is 256×128×128 corresponding to pixel size of 0.39 × 0.78 × 0.78mm. Fibre orientations (see Figure 1E, F) were obtained from diffusion tensor MRI (DT-MRI) in a 7.1 T MRI scanner. These data were then segmented into a hexahedral mesh, consisting of cardiac tissue and cavities (see Figure 1C). The data was manual segmented to functional modules according to the known anatomical structure of canine heart (see Figure 1D). The volume of the canine ventricular data matrix comprised of 398,446 nodes.

2.2. Electrical activation propagation

The normal contraction patterns of heart may be affected by abnormal conduction of the depolarization wave. Cardiac tissue was assumed to be anisotropic. Conductive wave velocity was higher parallel (0.41 m/s) than perpendicular (0.15 m/s) to the myofibre [3]. The dynamic ionic model developed by Winslow et al. was used to simulate the electrophysiology of a single ventricular cell [4]. The electrical activation conduction sequences were simulated based on solutions of reaction-diffusion equations and with a strategy of parallel computation.

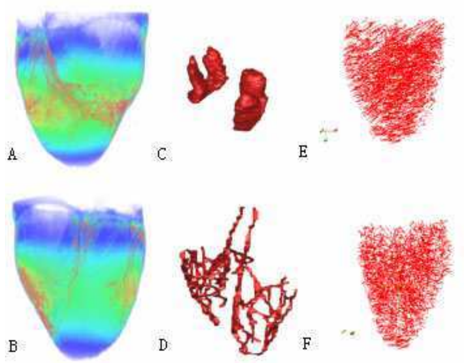

Figure 1. 3D view of the canine ventricular anatomical model. The left panel (A, B) shows 3D view of the whole ventricles scanned at Duke University Center visualized by Volview® 2.0. C and D show the reconstructed cavities and conduction system of the canine heart model. E and F display the fibre angles (E is front view, F is right view).

Figure 2 shows the simulated activation sequences of LBBB and RBBB. Latest depolarization of LBBB and RBBB occurred at 108 ms and 90ms respectively.

2.3. Mechanical properties of cardiac tissue

Passive and active mechanical properties of cardiac tissue have been considered in this investigation. Passive myocardial material was considered anisotropic and nonlinearly elastic as Kerckhoffs did [2]. A modified mathematical model, proposed by Guccione and McCulloch, was used to predict active tension developed by cardiac muscle fibre [5].

In the fiber-coordinate system (one axis is chosen to coincide with the local muscle fibre direction, another one is determined by the epicardium surface normal vector), the nodal force vector of each element $\{F_f\}^e$ in the direction of fiber is shown in Equation (1).

$$\{F_f\}^e = -\sum_{l=1}^{L_e}\int_{\xi_{l-1}}^{\xi_l}\int_{-1}^{1}\int_{-1}^{1}[B]^T T\{0,0,\sigma_e,0,0,0\}_l^T |J|\, d\xi d\eta d\zeta \tag{1}$$

where $[B]$ is the geometric matrix of an element, σ_e is the active myofibre stress as a function of peak intracellular calcium ion concentration, time after onset of contraction and sarcomere length history time, $|J|$ is the determinant of the Jacobin matrix, ξ, η, ζ are the local coordinate system with the magnitudes ranging from -1 to 1, l and L_e are the number and total number of layers in an element, respectively and T is the transformation matrix between the fiber coordinate and global coordinate.

After the excitation series were determined, these constitutive relations for cardiac mechanics will then be incorporated into a continuum electromechanical heart model to predict wall motion and deformation based on the finite-element method (FEM).

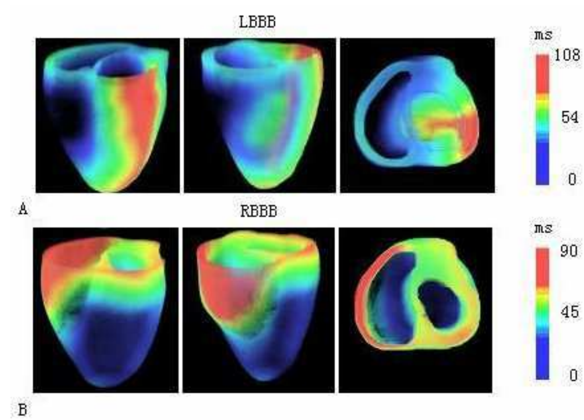

Figure 2. Isochrones of simulated BBB activation in different views of the canine ventricles. Panel A for LBBB and panel B for RBBB.

2.4. Finite-element method

For the operation of convenience, the LV and RV walls are divided into 14 layers from apex to base along the long axis in this model. There are in total 2269 hexahedral elements and 8736 degrees of freedom. After discretizing the ventricles into finite elements in radial direction, we group ten layers per element and assume that all the fibers within a layer are in the same orientation. Thus, the active force vectors are multi-directional inside an element.

A Windkessel model for arterial impedance was coupled to ventricular pressure to compute the homodynamic boundary and pre-load was also added. The equations related to mechanics are solved using a Galerkin finite-element method with eight-node isoparametric elements. Regional motion and deformation of the ventricles are then calculated during systole phase.

3. Results

3.1. Motion of ventricles

In the ventricular wall movement simulation of LBBB, the result shows that when the RV starts to contract during early-isovolumic contraction, the LV free wall is still in its relaxation phase, causing an abrupt posterior motion of the interventricular septum. The delayed onset of LV contraction, occurring at the septum begins to relax, resulted in a paradoxical septal-LV movement, which lead to a decreased septal contribution to stroke volume. Such results are in good accordance with experimental findings reported by others [6]. For the RBBB simulation, the opposite is observed: LV enters the ejection phase first with a delayed paradoxical septal-RV movement.

3.2. Ventricular minimum principal strain

The minimum principal strain*, E3,* as an index to represent the physiological phenomenon of muscular contraction [7], was used to describe the mechanical deformation of ventricles.

Figure 3 shows the distribution of *E3* at RV endocardium and LV mid-wall for LBBB (top panels) and RBBB (bottom panels) during ejection respectively. The reference state was set at the beginning of systole. Notice that *E3* increased with the increase of time, indicating the compression of ventricles.

RBBB simulation shows that the septum of RV begin to contract earlier than RV free wall during ejection as shown in Figure 3C, while there was a consistent contraction of LV in Figure 3D. On the contrary, in LBBB simulation, there was an obvious inconsistent contraction of LV during ejection, as shown in Figure 3A and Figure 3B. Computed strains also showed that the heart is associated with prolonged systolic activity by increasing pre-ejection time in LBBB compared with RBBB, as observed in Figure 3 [1]. Further more, the peak value of *E3* in RBBB is larger than that in LBBB, which lead to more decreased stroke volume in LBBB. Therefore, patients with RBBB may have more mechanical synchrony and better systolic function.

3.3. The first main stress distribution within cross section of ventricles

The stress distribution within cross section of ventricles around equator site during ejection was calculated and shown in Figure 4. Figure 4A shows that RV free wall and septum have a higher stress than LV free wall in LBBB during ejection. In RBBB, stress develops rapidly in the myofibres of LV (Figure 4B), which lead to a quick increase of ventricular pressures. The predicted peak stress of RBBB has a higher magnitude than that of LBBB.

3.4. Ejection fraction (EF) analysis

A measure of the function of left ventricle, also called left ventricular ejection fraction (LVEF), can help to determine if systolic or diastolic heart failure is present. A normal ejection fraction is 50% or higher. An ejection fraction of less than 40 percent usually confirms systolic heart failure. LVEF is defined as

$$LVEF = (EDV - ESV) / EDV \qquad (2)$$

where *EDV* means *LV* volume of end-diastole while *ESV* represents the *LV* volume of end-systole.

Simulations show that LVEF in LBBB (21.7%) is lower than that in RBBB (24.7%), which revealed a more decreased ventricular function and hemodynamics deterioration in LBBB.

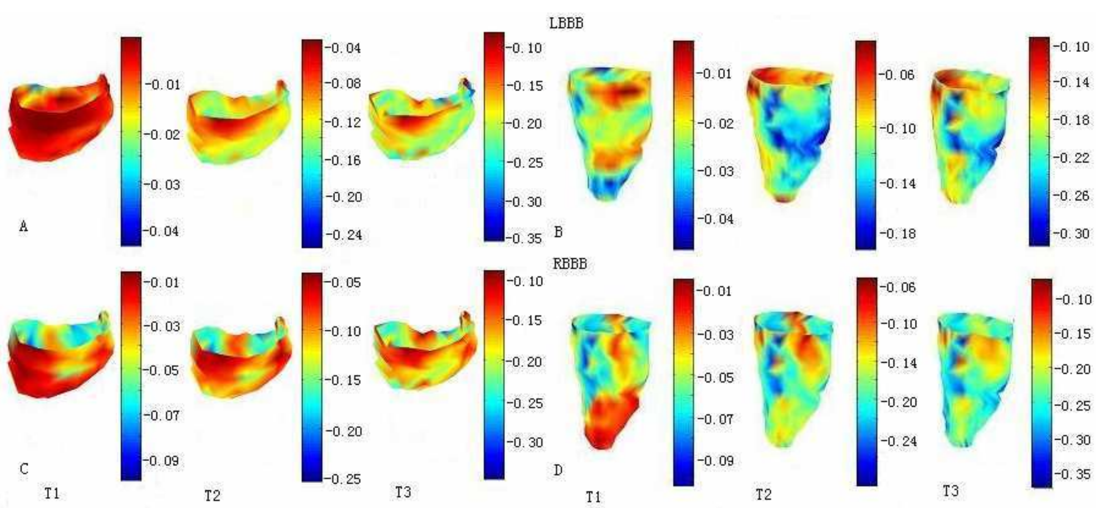

Figure 3. The negative *E3* of RV endocardium and LV mid-wall in LBBB (panel A, B) and RBBB (panel C, D) at three

different times (T1: end-isovolumetric contraction; T2: middle-rapid ejection; T3: begin-reduced ejection).

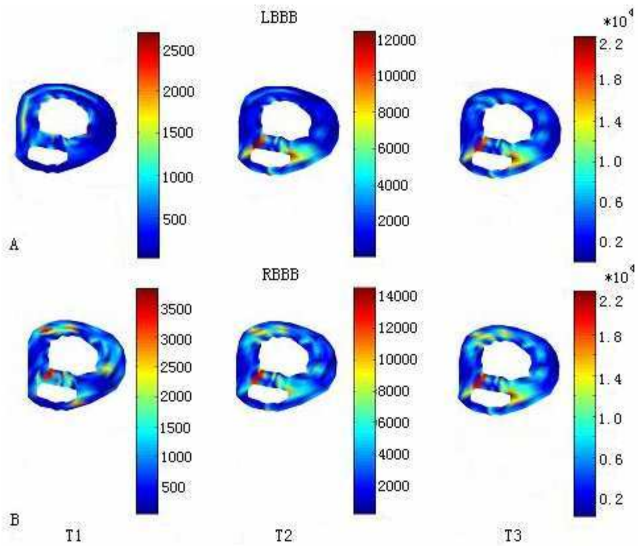

Figure 4. The first main stress distribution of ventricular walls in layer 8 around equator site of ventricles during LBBB (panel A) and RBBB (panel B).

4. Discussion and conclusions

The simulated distribution of strains and stresses of ventricular walls demonstrated that there is an asynchronous contraction of the septum, the LV and RV free walls during BBB. The loss of septal contribution may result in a reduction in global ejection fraction in BBB. These results are in good accordance with experimental findings reported in the literatures [1,6].

LBBB may result in a more pronounced asynchrony of contraction accompanied by increased energy consumption in the myocardium, which may explain why patients with isolated LBBB have higher mortality rates than those with isolated RBBB and are more likely to develop advanced cardiovascular disease [8-9].

In conclusion, the mechanical properties of BBB have been simulated based an electromechanical canine heart model, and the simulation results are in good accordance with experimental findings reported in the literatures. This investigation suggests that such a model is able to serve as a building block for developing the more perfect heart models, and may be used to optimize timing and location of ventricular pacing for cardiac resynchronization therapy (CRT) [10].

Acknowledgements

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References

[1] Usyk TP. Forward Modeling of Ventricular Electromechanical Interactions: Normal and Failing Hearts. Proceedings of the 26th Annual International Conference of the IEEE EMBS 2004:3563-3564.

[2] Kerckhoffs RCP, Faris OP, Bovendeerd PHM, Prinzen FW, Smits K, McVeigh ER, Arts T. Electromechanics of paced left ventricle simulated by straightforward mathematical model: comparison with experiments. Am J Physiol Heart Circ Physiol 2005:289:1889-1897.

[3] Thomas SA, Schuessler RB, et al. Disparate Effects of Deficient Expression of Connexin43 on Atrial and Ventricular Conduction: Evidence for Chamber-Specific Molecular Determinants of Conduction. Circulation 1998;97: 686-691.

[4] Winslow RL, Rice J, et al. Mechanisms of altered excitation-contraction coupling in canine tachycardia-induced heart failure, II: model studies. Circ Res 1999;84:571-586.

[5] Guccione JM, McCulloch AD. Mechanics of active contraction in cardiac muscle: Part !-Constitutive relations for fiber stress that describe deactivation. J of Biomech Eng 1993;5:72.

[6] Liu LL, Tockman B, Girouard S, Pastore J, Walcott G, KenKnight B, Spinelli J. Left ventricular resynchronization therapy in a canine model of left bundle branch block. Am J Physiol Heart Circ Physiol 2002;282:2238-2244.

[7] Liu F, Lu W, Xia L, Wu G. The construction of three-dimensional composite finite element mechanical model of human left ventricle. JSME Int. J. 2001;44:125–133.

[8] Zannad F, Huvelle E, Dickstein K, van Veldhuisen DJ, Stellbrink C, Køber L, Cazeau S, Ritter P, Pietro A Maggioni, Ferrari R. Left bundle branch block as a risk factor for progression to heart failure. European Journal of Heart Failure 2003; 9:7-14.

[9] Norbert M, van Hemel. Left is worse than right: the outcome of bundle branch block in middle-aged men. European Heart Journal 2005:26:2222-2223.

[10] Miri R, Reumann M, Farina D, Osswald B, Dössel O. Optimizing A-V and V-V Delay in Cardiac Resynchronization Therapy in Simulations Including Ventricle Heterogeneity. Proceeding of Biomedical Engineering 2007:555.

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