

Computational model of heart remodeling following relief of hemodynamic overload in a biventricular canine heart model

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Computational models with the ability to predict the time course of growth and remodeling of the heart could have useful clinical applications. Specifically, the ability to predict a patient-specific growth trajectory can help surgeons make informed decisions on when to perform procedures. Current state-of-the-art cardiac growth models are able to predict patterns of hypertrophy in response to various hemodynamic perturbations including pressure overload (PO, induced by aortic banding) and volume overload (induced by mitral regurgitation or arteriovenous fistula). Key clinical questions, however, often involve whether and how the heart will reverse remodel following an intervention. Therefore, the objective of this study was to evaluate the ability of a cardiac growth model [1] to predict reverse remodeling following PO. To this end, we compared model predictions of forward and reverse growth to reported experiments [2], where PO was induced in dogs via aortic banding for 18 days followed by removal of the band for 1-7 days.

We utilized a previously published framework consisting of a finite-element model of a beating biventricular canine heart with a realistic myofiber structure, coupled to a nonlinear lumped-parameter model of the systemic and pulmonary circulation [1]. We ran the coupled normal (baseline) model to a hemodynamic steady state and calculated baseline strain values in the heart. Aortic stenosis (PO) was simulated by changing the simulated area of the aortic valve and the systemic vascular resistance to match reported acute hemodynamics immediately following banding. For each growth step, new strain values were calculated, the growth law [1] was applied, and the grown model was coupled to the circulation and run to a hemodynamic steady state. Growth in the fiber direction was driven by changes in maximum fiber strain from baseline while growth in the radial/crossfiber directions was driven by changes in minimum first principal strain in the plane perpendicular to the fibers. We ran 12 forward growth steps (equivalent to 18 days) under PO, which was then relieved by restoring the circulation parameters for the baseline model and run for 4 reverse growth steps (equivalent to 6 days).

Our model matched the experimental increase in maximum LV pressure with banding and decrease following unloading. Throughout forward growth, the model predicted ~10% radial and ~4% fiber growth on average across elements in the LV freewall. Following PO relief, LV pressures returned to baseline while LV volumes and global stretches remained elevated; thus, the model predicted little reverse remodeling. These growth patterns resulted in model predictions of LV ED wall thickness and diameter that were in agreement with experimental data at all time points [2]. Since the experimental data used for comparisons here followed animals for a very short time after relief of PO, future work will include examining model predictions over longer durations of overloading and unloading.

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References: [1] Kerckhoffs, RCP et al., *Mech. Res. Commun.*, 2012; [2] Sasayama et al., *Circ. Res.*, 1976.