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Computational Model of Heart Remodeling Following Relief of Hemodynamic Overload in a Biventricular Canine Heart Model

Cardiac Biomechanics Group

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Introduction

- Current cardiac growth models are able to predict patterns of hypertrophy in response to various hemodynamic perturbations such as concentric hypertrophy in pressure overload (PO) and eccentric hypertrophy in volume overload (VO)
- Computational models with the ability to predict patient-specific time courses of growth and remodeling of the heart could have useful clinical applications
- Key clinical questions, however, often involve whether or how the heart will reverse remodel following an intervention

Objective: Evaluate the ability of a cardiac growth model [1] to predict reverse remodeling in a canine model of pressure overload (PO) [2].

Methods

Finite element (FE) model:

- We utilized a framework consisting of a beating biventricular canine heart with realistic myofiber structure, coupled to a lumped parameter model of the systemic and pulmonary circulation (CircAdapt) [1].
- Hill-type active and Fung-type passive mechanics were modeled for the myocardium.
- Simulations were conducted in Continuity v.6.4b

Cardiac growth law [1]:

- Fiber axial growth (lengthening) is driven by:
  - Δ in maximum fiber strain from baseline levels.
  - Usually occurs at diastole.
- Cross-fiber and fiber radial growth (thickening) is driven by:
  - Δ in minimum of 1st principal strain of the cross-sectional strain from baseline levels.

$$E_{cross} = \begin{bmatrix} E_{cc} & E_{cr} \\ E_{cr} & E_{rr} \end{bmatrix}$$

  - Usually occurs during systole

Growth simulation and model validation:

- For baseline, acute, and all growth simulations, the FE model was coupled to the circulation model and run to a circulatory steady state
- Aortic stenosis (PO) was simulated by reducing the circulatory parameter associated with the aortic valve area. These parameters were kept consistent for 12 forward growth steps (~18 days).
- After forward growth, circulatory parameters were returned to baseline values, and models were run for 3 reverse growth steps (~5 days)
- Model predictions were compared to experimental data from [2].

Results

Hemodynamics

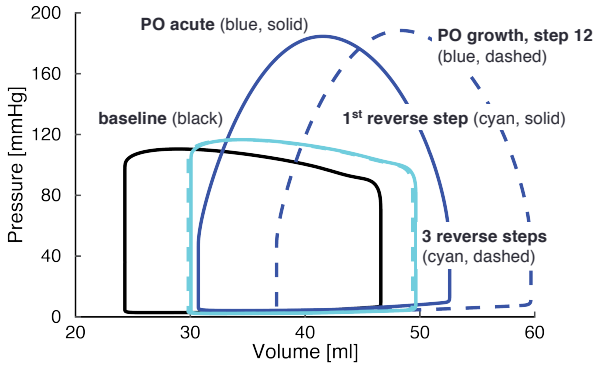

Figure 1: Returning circulation parameters to baseline levels after growth caused max LV pressures to return to baseline levels and end-diastolic pressures to drop below baseline levels. Left ventricular pressure-volume loops for baseline, acute PO, forward, and reverse growth.

Stimuli changes

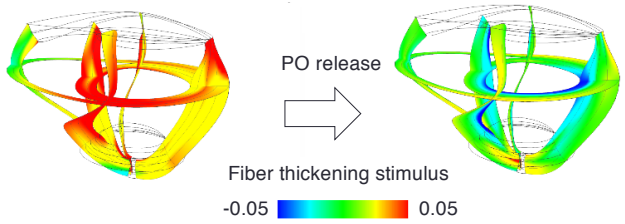

Figure 3: The model predicted little reverse remodeling because strains dropped to (but not below) baseline values with unloading. Fiber thickening stimulus at the end of forward growth is high as indicated by yellow and red. When PO is released, stimulus values drop to near zero indicated by green, indicating that elastic strains return to baseline strain values.

Hypertrophy

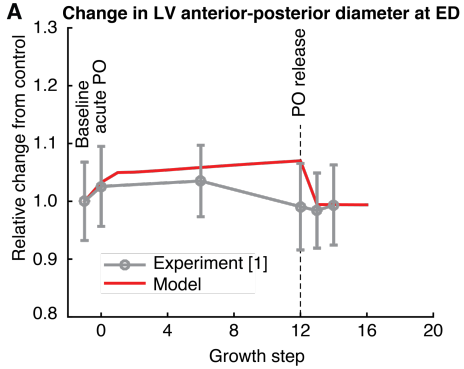

Figure 2: Model-predicted changes in LV dimensions matched experimental results from [2]. A) LV anterior-posterior cavity diameter. Our model predicted an average of 4% radial growth and little reversal after PO release. B) LV lateral wall thickness at end-diastole. Our model predicted an average of 10% radial growth and little reversal after PO release.

Conclusions

- Our model matched the experimental increase in maximum LV pressure with banding and decrease following unloading.
- Predicted changes in LV dimensions were in agreement with experimental data.
- Following unloading, pressures returned to baseline values but strains did not; thus, the strain-based growth law did not predict reverse remodeling.

References

[1] Kerckhoffs, RCP et al, Mech. Res. Commun, 42:40-50, 2012.
[2] Sasayama S. et al, Circ Res 38:172-189, 1976.

Acknowledgements

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