Appendix 1A

The formulation for the Ca transient in the myofilament model was modified to reflect abnormal Ca handling associated with DHF, namely the peak Ca amplitude was reduced by 40% and the time for decay of the Ca transient to its half-maximal value was increased by 40% from the corresponding values in the normal canine ventricles; the latter values can be found in Provost et al.[1] Modified parameters in the representation of the Ca transient in Rice et al. model include:

$\tau_1 = 0.035\text{s}$

$\tau_2 = 0.17\text{s}$

$\text{Ca}_{\text{amplitude}} = 1.0\mu\text{M}$

$\text{Ca}_{\text{peak}} = 0.7\mu\text{M}$

The modified formulation of the Ca transient in Rice et al. model is as follows:

$$\beta = \left(\frac{\tau_1}{\tau_2}^{-1/\left(\frac{\tau_1}{\tau_2}-1\right)} - \frac{\tau_1}{\tau_2}^{-1/\left(1-\frac{\tau_2}{\tau_1}\right)}\right)$$

$$\text{Ca}_t = \begin{cases} \text{Ca}_{\text{diastolic}} & \text{for } t \le t_{\text{start}} \\ min\left\{\left(\frac{\text{Ca}_{\text{amplitude}} - \text{Ca}_{\text{diastolic}}}{\beta}\right)\left(e^{-\frac{t-t_{\text{start}}}{\tau_1}} - e^{-\frac{t-t_{\text{start}}}{\tau_2}}\right) + \text{Ca}_{\text{diastolic}}, \text{Ca}_{\text{peak}}\right\} & \text{for } t > t_{\text{start}} \end{cases}$$

Appendix 1B

In this study, the formulation for the mitral flow in the model of the circulatory system was modified as follows. Backward flow from LV to LA was allowed when pressure in LV (P_{LV}) was higher than that in LA (P_{LA}). Regurgitant flow was formulated as the

pressure difference between LV and LA divided by the product of mitral valve resistance and the scaling factor for mitral valve resistance.

$$Q_{mitral} = \begin{cases} \dfrac{P_{LA} - P_{LV}}{R_{mitral}} & P_{LA} \geq P_{LV} \\ \dfrac{P_{LA} - P_{LV}}{R_{mitral} \times MR_{factor}} & P_{LA} \leq P_{LV} \end{cases}$$

where MR_{factor} is the scaling factor for mitral valve resistance

The scaling factor for mitral valve resistance was set to 500 so that the mitral regurgitant fraction, the ratio of the regurgitant volume to mitral inflow volume, was 31% in the model of the DHF ventricles, consistent with the mitral regurgitant fraction measured experimentally in failing ventricles.[2]

1. Provost J, Gurev V, Trayanova N, Konofagou EE. Mapping of cardiac electrical activation with electromechanical wave imaging: an in silico-in vivo reciprocity study. Heart Rhythm 2011;8:752-759.

2. Kanzaki H, Bazaz R, Schwartzman D, Dohi K, Sade LE, Gorcsan J, 3rd. A mechanism for immediate reduction in mitral regurgitation after cardiac resynchronization therapy: insights from mechanical activation strain mapping. J Am Coll Cardiol 2004;44:1619-1625.