**Model-based Cardiovascular Therapeutics: Capturing the patient-specific impact of inotrope therapy**

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**Abstract**:

**Introduction**: A model for the cardiovascular and circulatory systems (CVS) has previously been validated in silico, as well as in porcine models of pulmonary embolism (PE), septic shock, and positive end-expiratory pressure (PEEP) titrations at different volemic levels. An accurate CVS system model can be used to monitor and diagnose dysfunction and support clinical decisions. This research validates this model with respect to inotrope therapy commonly used in circulatory support, prior to first human clinical trials.

**Method**: The model and parameter identification process is used to study the effect of different adrenaline doses in healthy and critically ill patients. The hemodynamic effects on arterial blood pressures and stroke volume (cardiac index) are simulated in the model and adrenaline-specific parameters identified. These parameters are then used to capture and predict the future responses to a change in dose and-or over time. Results are compared to clinical data from 3 adrenaline published dosing studies, comprising a total of N=37 data sets.

**Results**: All identified parameter trends match clinically expected changes. The adrenaline-specific parameters are physiologically relevant. Absolute percentage errors for the patient-specific, predicted hemodynamic responses (N=15) are within 10% compared to clinical data. The adrenaline-specific parameters accurately and uniquely capture the impact of inotrope therapy on the CVS, independent of other model parameters.

**Conclusions**: Clinically accurate prediction of the impact of circulatory support drugs, such as adrenaline, offers significant clinical potential for this type of model-based application. Overall, this work represents a further clinical validation of the underlying fundamental CVS model and methods, and their use for cardiovascular diagnosis and therapy selection in critical care. These results are presented as (further) justification for (beginning) human trials of this model-based diagnostic and therapeutic approach.